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PRESENT STATUS OF ULTRASOUND IN MEDICINE

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• *Generators of ultrasonic vibrations for medical purposes usually supply a frequency of 800 to 1,000 kilocycles per second, at intensities ranging up to a maximum of 2.5 to 3 watts per square centimeter. The destructive effects of higher intensities are well known, but it is doubtful whether they will prove useful for the removal of tumors, disintegration of calculi, or destruction of bacteria in foci of infection. Nondestructive doses are a welcome addition to the measures used to relieve painful conditions in the neuromuscular and skeletomuscular systems. Ultrasound can be used either by the transsonation or by the echo-ranging technique to outline deep-lying masses of soft tissue, whether normal or diseased; it has therefore shown promise of diagnostic application.*

Ultrasound as a therapeutic modality in medicine was introduced to the United States in 1949. Coming from the European continent where it had enjoyed its reputation of an efficient therapeutic modality, ultrasound was received in the United States by some with considerable enthusiasm and by most with reluctance and suspicion. This suspicion was rightly based on the many unsubstantiated claims regarding the therapeutic efficacy of this new physical energy. The reluctance, however, was unjustifiably caused by certain known destructive lesions that can be produced intentionally in experimental studies and that could also occur unintentionally if this agent were unjudiciously used in doses higher than those established for therapeutic application. Today, overenthusiasm and prejudice have given way to a more even temper with which ultrasound can be discussed. In medicine, the applicability of ultrasonics concerns itself with four phases: (1) as an experimental laboratory device, (2) as a radiant energy in physical therapy, (3) as a selectively destructive agent, and (4) as a diagnostic tool.

In spite of continual research in laboratory and clinic, much of the knowledge regarding ultrasonics remains hypothetical. Publications in the international as well as in the English-language journals have reached the thousands, but, instead of clarifying the knowledge of ultrasonic effect, many of the publications have added to the confusion. A complete review of the present status of ultrasound is outside the scope of this paper. Also, it is questionable whether a complete, all-encompassing presentation would fulfill the purposes of this paper, which are to present the highlights in the use of ultrasound in medicine, especially from the viewpoint of more recent work; to introduce the subject to those who have not been exposed to a knowledge of ultrasound; and to review the field for those who have previously been interested.

This can best be done by presenting only the most pertinent contributions. Failure to include any other publications, however, should not be construed by the respective authors as a criticism of their work or as an indication that it is not considered valuable. I have tried before to review the field and to introduce its therapeutic possibilities and rationale.[1]

Physics

The general interest in ultrasonics is understandable if one considers that ultrasound, also called nonaudible sound, is a physical energy that is completely different from all other radiant energies. It is not represented in the electromagnetic spectrum; it depends for its production and transmission on matter and—at least theoretically—changes any matter in its path from a mechanically quiet into an oscillating state. This apparently is a characteristic physical property of ultrasound, though this physical phenomenon does not explain its therapeutic effect. Other biophysical differences between sonic energy and the other radiant energies, used in medicine, are the inability of ultrasound to penetrate a vacuum, or to pass through an interface of two mediums having widely different acoustic characteristics (such as air and solids), and its capacity to produce at such interfaces important physical interference phenomena (such as deflection, reflection, and absorption). Physically, audible and non-

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audible sound are identical energies, their difference being based solely on their frequency of oscillation. The human ear, depending on the age of the person and on individual ability, can perceive as audible sound oscillations of frequencies as high as 16,000 to 20,000 cps; therefore, any acoustic energy above 20,000 cps is called nonaudible, or ultrasound.

All electromagnetic frequencies are transverse waves, moving with the speed of light, while acoustic oscillations are longitudinal waves consisting of rhythmic alternations of compression and rarefaction of matter (fig. 1). As a result, the speed of sound changes

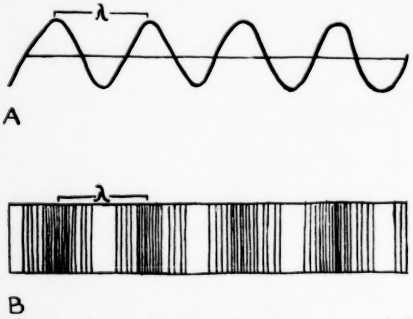

Fig. 1.—Schematic drawing of, *A*, transverse wave and, *B*, longitudinal wave (λ=wave length).

considerably, depending on the mediums to be traversed; it is slowest in gases, faster in liquids, and fastest in solids. Recently the velocity of high-frequency sound in mammalian tissues has been tabulated by Goldman and Hueter[2] from their own studies as well as from data supplied by other investigators.

Medical ultrasound apparatus supply a frequency of 800 to 1,000 kilocycles per second. This is a compromise between lower frequencies with better penetrating power and still higher frequencies with greater absorbability. The energy can be produced by a variety of mechanisms, such as ultrasonic whistles and sirens, magnetostrictive devices that utilize the rhythmic expansion and contraction of a metal rod within the electromagnetic field, and finally by piezoelectric apparatus, which are the most suitable equipment for medical ultrasound. The piezoelectric effect consists of the production of an alternating high-frequency electric current at the opposing surfaces of a quartz crystal, which undergoes mechanical pressure changes by rhythmic compression and release. Reversely, the ultrasound generators charge the opposing surfaces of a quartz crystal with high-voltage, high-frequency currents, thus producing rhythmic mechanical oscillations at the surface of this crystal. The quartz crystal is encased in a so-called sound or treatment head, which is connected to the high-frequency generator by a coaxial cable. In some equipment synthetic crystals are used instead of quartz (fig. 2).

Biological Phenomena

One of the most complete reviews of ultrasound in medicine in the American literature was published by Nelson, Herrick, and Krusen.[3] In their paper they discussed the various biological phenomena observed in tissues and test animals. Since most of the laboratory studies were done with destructive doses, the authors at that time concluded that ultrasound was too dangerous an agent to be used generally as a therapeutic modality. However, today there is complete agreement that, if used by trained medical personnel, ultrasound is a safe therapeutic device. Biological experiments have been carried out chiefly in order to explain the effect mechanism of ultrasound. Apparently, the ultrasonic effect, as seen in laboratory studies, is due to mechanical influences of the rhythmically oscillating acoustic energy as well as to heating caused by absorption and conversion of energy. In nondestructive therapeutic doses the ultrasonic effect is probably solely thermal. However, hoping to find ultrasound to be an energy completely different from other physical therapeutic modalities, a few investigators have tried to explain their clinical observations exclusively or chiefly on the basis of mechanical phenomena. Most investigators have compromised by stating that the therapeutic effect of ultrasound is chiefly thermal and possibly also mechanical.

In a well-grounded study, Lehmann and his co-workers[4] proved the existence of both the thermal and the mechanical effects. They could demonstrate on the chromosomes and other structures of the cells of plant tissue that two types of destruction could be differentiated. The one caused by thermal effects was suppressible by cooling, and the other caused by mechanical stresses could be avoided by careful compression. This mechanical damage is the result of either cavitation or pseudo-cavitation, which means the formation of cavities within the sonated medium by actual tearing or liberation of gases respectively. However, when observing the ultrasonic effect with nondestructive doses, Lehmann and his co-workers[4]

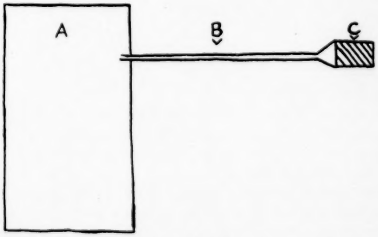

Fig. 2.—Schematic drawing of ultrasound generator. *A*, oscillator; *B*, coaxial cable; *C*, quartz crystal.

consistently found that the heating effect is quantitatively dominant and the mechanical component questionable or of minor importance. This conclusion is based on their work with membranes and observation of ion transport through biological membranes. Paul and Imig[5] confirmed this opinion in their studies on blood flow. Gersten[6] demonstrated physiological changes on tendons that he also found to be dependent on temperature or reproducible by mere heating.

Physical Therapeutic Application

Like roentgen rays, ultrasonic radiation has been used therapeutically in destructive and nondestructive doses. The application of destructive ultrasound, however, is essentially still at the experimental stage. The difference between destructive and nondestructive therapy depends entirely on dosage. There is no consensus yet regarding an optimal dose, and the recommended therapeutic dosage is entirely empirical. It is difficult—or impossible—to determine a therapeutic dose of a physical agent through observations on mice or frogs, but it seems safe to assume that human tissue is able to tolerate at least as much energy as that of small experimental animals.

The dose is dependent on both the sound intensity at the surface of the transmitting sound head and the duration of the treatment. The intensity is selected according to the treatment method. There are three methods of treatment: 1. The stationary method, whereby the treatment head remains in place, requires the lowest intensity, but it has the disadvantage of presenting the greatest possibility for interference and of allowing the treatment of only a small area. 2. The slightly moving sound head method, which eliminates interference phenomena and therefore permits somewhat larger doses, is still applicable to a small area only. 3. The moving or massaging sound head method, whereby the transducer is moved over the part to be treated, permitting largest doses and the treatment of large areas, allows the sound intensity to be determined by the thickness of the soft tissue overlying the anatomic parts to be treated; the time element of the dosage is dictated by the size of the area. The moving sound head method is now used almost exclusively in the U. S. Intensities range up to a maximum of 2.5 to 3 watts per square centimeter. It should be noted that in treatment with the moving sound head the size of the transmitting surface is of some importance, since the larger the sound head diameter the more often the individual tissue elements will be exposed during the treatment period. The presence of burning, increased pain, or any undue discomfort during the treatment is a definite warning signal indicating overdosage. Report of such sensations by the patient must immediately be followed by reduction of the intensity.

Nondestructive ultrasonic therapy has been recommended for many conditions but has chiefly been applied in the treatment of rheumatic, inflammatory, and traumatic lesions of the neuromuscular and musculoskeletal systems. As is the case with all physical therapeutic agents, the evaluation of the therapeutic efficacy of ultrasound meets with certain difficulties due to the nonspecificity of this agent and the nature of the conditions being treated. These are chiefly diseases that are self-limited in many instances or characterized by spontaneous remissions. That favorable results have been reported in these conditions is not surprising, since the therapeutic mechanism is based on hyperemia, which is the result of the heating effect of ultrasound either alone or in conjunction with other biophysical phenomena.

Actually, among those who have used ultrasonic therapy there seems to be complete agreement that ultrasound is a valuable therapeutic device. However, whether it is more efficient than other therapeutic agents still remains problematic. If ultrasound is evaluated by comparing results with its use with results in therapeutically neglected control patients, its efficacy appears to be much higher than if the control patients are treated with other known physical therapeutic agents, in which case the end-results are statistically similar.[1]

To my knowledge, ultrasound cannot improve or remedy any conditions that heretofore were not amenable to other forms of treatment. Likewise, conditions that can be improved only symptomatically (such as rheumatoid spondylitis) also cannot be cured by ultrasonics. Scleroderma and multiple sclerosis, for instance, were reported to respond to ultrasonic therapy, but there has been no proof or evidence to that effect. Painful stump neuromas and phantom limb pain, which are known for their resistance to any form of therapy, reportedly responded well to ultrasound.[7] However, in my attempts to influence neuromas, I have not been able to obtain such favorable results.

The following conditions have shown worthwhile responses to ultrasonic therapy according to my experience: strains and sprains; low back strain, acute and chronic; fibrositis; myositis; tendinitis; tenosynovitis; olecranon bursitis; subdeltoid bursitis; humeroscapular periarthritis; sciatic neuralgia and other neuralgias; radiculitis; and ankylosing (Marie-Strümpell) spondylitis.

Ultrasonic therapy should not be considered a panacea and is contraindicated whenever its use would delay the application of other forms of proved therapy. This is especially true for malignant tumors, which constitute a definite contraindication not only because of such a delay but also because local growth of the neoplasm and metastatic spread have been observed after ultrasonic therapy.

Furthermore, the sonation of certain organs is contraindicated due to the potential danger of ultrasonic energy. The many existing interfaces of the eye could become subject to hemorrhage as the result of interference phenomena. The gonads supposedly are especially sensitive to ultrasound, and the pregnant uterus should not be sonated because of the danger of abortion that exists with any form of radiation. Rhythm changes of the heart have been reported as undesirable side-effects during sonation of the heart and the stellate ganglion. Hemorrhages may occur in patients with large peptic ulcers or with advanced stages of bronchiectasis if ultrasound is used. It should not be used in anesthetized patients or those under heavy sedation, as they are unable to report undue pain and burning, the safety mechanism against overdosage. Anesthetic skin areas should be treated guardedly, if at all. Finally, it must be emphasized that locally applied ultrasound, like any form of thermal therapy, is definitely contraindicated in the case of arterial insufficiency of the extremities.

Destructive Ultrasonics

Destructive doses have been used experimentally and clinically for the treatment of tumors. Horvath[8] was the first investigator to report on human skin cancers cured by ultrasonation. However, for reasons

stated above, it is generally agreed that ultrasound therapy for cancer in humans is not permissible. More recently, Woeber [9] demonstrated that a combined ultrasound and x-ray therapy regimen for tumors was capable of reducing the x-radiation dose by 40%, in comparison with x-ray therapy alone. In similar studies Lehmann and Krusen [10] reported a saving of as much as 50% of the x-ray dose. This saving was dependent upon the thermal effect of ultrasound; no reduction of x-ray dose was possible when the experiments were performed under cooling. These investigators observed that the destructive effect of ultrasound on tumor tissue was greater than that of diathermy, since ultrasound can be focused and is readily absorbed at the multiple interfaces of the tumor tissue.

This combination tumor therapy is still in its experimental stages and is applicable only to easily accessible skin or subcutaneous neoplasms. The desirability of reducing the x-ray dose in favor of another physical agent appears to be quite questionable.

Ultrasound has also been used, experimentally as well as therapeutically, for the destruction of normal brain tissue. Lindstrom [11] reported that in his work with patients with incurable conditions he applied ultrasonic energy through frontal bur holes for the purpose of obtaining brain lesions that produced equal or better results than surgical leukotomies. Fry and associates [12] have developed an apparatus that is capable of focusing high-intensity ultrasound into small areas. They sonated the brain of monkeys through craniotomies and were able to destroy small areas at various depths without injuring the cerebral cortex. White matter was reportedly more readily affected, and higher doses were required for obtaining changes in gray matter. Selective accurately positioned lesions as small as 2 to 3 mm. in maximal diameter could be produced at any desired depth without affecting the intervening tissue. Since blood vessels were found to be most resistant to ultrasound, it was possible to destroy fiber tracts without destroying gray matter or damaging the blood circulation. This type of ultrasonic surgery is of no practical value yet. Its therapeutic applicability has to await further studies; its importance would be greatly enhanced if transcranial sonation were possible.

Because of the mechanical action of ultrasonics, the destruction of calculi has been experimentally attempted with this energy. Lamport and co-workers [13] were able to fragment biliary stones that were sonated in cellophane bags. In later experiments in animals, they placed these calculi in exteriorized loops of intestine that were filled with saline solution. More recently these authors described a special ultrasonic sound head to which was attached a probe-like drill for intraureteral fragmentation of stones. These experiments were successfully performed on stones placed in plaster replicas of ureters. Drilling of calculi was also possible in the ureter of the cadaver, but no actual lithotresis has been done in vivo.

Furthermore, ultrasound has been employed for the destruction of bacteria. The success of such destruction depends on the intensity of the sound, its duration, and the suspension fluid, which may have a protective function. The sensitivity of the different micro-organisms varies according to their type and strain; cocci are less sensitive than bacilli.[14] There is no evidence yet that this type of ultrasound therapy can be used for sterilizing abscesses, fistulas, and other infected areas in vivo.

Diagnostic Procedures

Ultrasound has been applied in industry for the detection of flaws in homogeneous material, such as steel and rubber. In medical diagnostics it has been used to visualize normal and pathological structures. Two techniques are available for this procedure: the transsonation method and the echo-ranging technique. In the transsonation method the object to be examined is placed between a transmitting sound head and a receiving sound head, both of which are physically identical. The transmitted acoustic energy is attenuated during its propagation through the examined object according to the structural characteristics of the latter. The attenuated sound then exerts its mechanical action upon the receiving crystal, which in turn translates this energy into electric frequencies; these can be made visible either on a cathode-ray oscilloscope or through a photographic method.

By using the transsonation method, Dussik [15] believed he had obtained an "ultrasonogram" that demonstrated the cerebral ventricles and brain tumors. However, Ballantine, Hueter, and Bolt [16] produced identical pictures by examining empty skulls; therefore, they concluded that Dussik's ultrasonograms did not represent intracranial structures but only the bony configuration of the skull and that it is not practical to obtain such pictures because of the varying thickness of the cranial bone.

More successful than the transcranial ultrasound examination seems to be the echo-ranging technique used by Homes and Howry and their associates.[17] Here, a single crystal serves as transmitter and receiver. These investigators were able to receive the echo of a single sound impulse as it returned to the transmitting crystal after being reflected from the various interfaces of the examined areas of the body. With this echo-ranging technique the investigators obtained pictures on an oscilloscope that were the result of thousands of ultrasonic pulses probing in various directions through the tissues. Due to the immense rapidity of this operation, it was possible to form a visually continuous picture on the oscilloscope. Thus, these authors were able to demonstrate "echograms" of a scirrhous carcinoma of the breast (not palpable prior to surgery); nonmetallic foreign bodies; cross sections of the neck; normal, cirrhotic, and metastatic liver tissue; and others. Until now only two-dimensional pictures have been demonstrated, but they believe that it should also be possible to develop a three-dimensional technique for stereoscopic viewing of the tissue. Wild and Reid [18] were able to utilize the same technique and diagnosed benign and malignant breast tumors in human beings with considerable accuracy with echograms.

Summary

From present knowledge it appears that ultrasound is applicable in medicine in the following areas: 1. In the biophysical laboratory ultrasound as an investigative tool seems to have considerable applicability. 2. In physical therapy there is sufficient evidence on hand

that ultrasonic therapy in nondestructive doses is a welcome addition for the relief of painful conditions of the neuromuscular and skeletomuscular systems. 3. In the treatment of tumors, the use of ultrasound in destructive doses is still experimental. At present, however, it seems more than doubtful whether it will ever play a major role in this field. Production of localized brain lesions has not been possible without craniotomy or bur holes; the practical value of such a procedure has not been established. Fragmentation of calculi has been done experimentally only. Destruction of bacilli has been demonstrated only in vitro. 4. In its diagnostic application for human diseases, ultrasound has shown promise, especially as far as the visual demonstration of soft tissues, pathological or normal, is concerned.

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EFFECT OF A CITY ON THE FALL-OUT OF POLLENS AND MOLDS

IMPLICATIONS FOR CIVIL DEFENSE

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• *Pollen counts were made in the air above and about a city on the west shore of Lake Michigan at a time when the wind was blowing from the southeast with a velocity of 7 knots (13 km. per hour). The counts involved Alternaria spores and ragweed pollen and were made at two different levels by airplane. The counts were found to be lowest north of the city, where they showed the combined effect of the air from the lake and rising air currents from the city. The conditions were duplicated experimentally by constructing a small model city, and it was shown that slightly warming the buildings caused air-borne Lycopodium spores to settle more densely over the rural areas about the city. This justifies the inference that the leeward parts of a city are safer than the country as regards radioactive fall-out after an atomic blast.*

Investigations have shown the rate of temperature change with altitude to be the most important factor in the rise and fall of pollens and molds.[1] These particles are held aloft by rising air currents when the air cools with increasing altitude, that is, when the temperature lapse rate is high and the air correspondingly unstable. The upward currents of warm air rising through colder air carry the particles into the clouds[2] or to a level where increasing altitude is no longer accompanied by a drop in temperature. The air is usually turbulent below the cloud level or the haze layer, and the solid particles reach their greatest concentration in this clearly visible layer. These particles are so sensitive to vertical currents of air that one degree of temperature has a measurable effect on their concentration at a certain level.[1]

The degree of fall-out of pollens and molds has been shown to be related to the time of the day or night. The greatest fall-out ordinarily occurs at night and early morning, when radiation from the earth causes the air to be cooler near the earth's surface and warmer above, the condition being termed a "temperature inversion."[1] At such times many people who suffer from asthma and hay fever experience their greatest discomfort, which they usually incorrectly attribute to dampness. Under these conditions the absence of upward currents favors fall-out. It is therefore not

surprising that a city, which is usually warmer than the surrounding country, should have a measurable effect on the distribution and fall-out of microscopic solid particles. This fact suggests both a natural and an artificial means of combating this hazard.

The method of collecting pollen on slides exposed from an airplane, which has been described,[2] has been improved. The microscopic slide coated with petrolatum is now held in position mechanically near the ventilator of an airplane, so that the timing and rapid changing of slides may be accomplished with ease and accuracy. We are able to collect as many solid particles in 30 seconds with this method as would be collected in 24 hours by the gravity or fall-out method.

A typical report of a survey, taken at 5:10 a. m., Aug. 22, 1954, includes the following information. There were scattered clouds at 15,000 ft. and thin broken clouds at 25,000 ft.; the visibility was 15 miles and the wind southeast at 7 knots (8.06 miles per hour). The dew point was 60 F, and the altimeter reading was 30.23 in. Hg. The ground temperature was 65 F, while the temperature at flight altitude (1,750 ft. above sea level or 1,000 ft. above the terrain) was 68 F.

An analysis of the number of particles in various sections of the city (fig. 1) indicates that the "country" pollen count is represented by the count made south of the city, on the windward side. The effect of the warmth of the city is found in the reduced pollen counts on the lee side, north and west of the city, rather than over the city itself (fig. 2). The consistently low counts to the east of the city reflect the effect of Lake Michigan.[3]

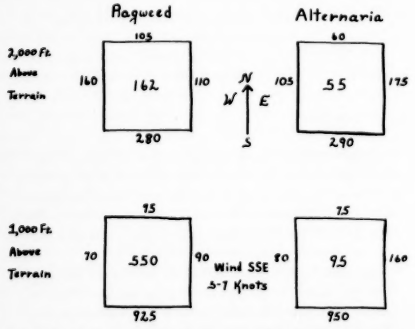

Fig. 1.—Diagram indicating counts of pollen and molds in vicinity of city. The squares represent the city. The upper squares show the counts of pollens and molds at the higher altitude and the lower squares the counts at the lower altitudes. The position of the numbers in the squares corresponds to the geographical location, showing the counts of particles on the four sides of the city and also over the city itself. The figures refer to the number of particles that impinge upon 1 sq. cm. of a microscopic slide in 10 minutes, the air speed remaining constant.

This survey was made during an inversion, that is, when the temperature at ground level was lower than that of the air above. Ordinarily this would have meant high pollen counts on the ground, since the conditions were favorable for fall-out. The counts over the country were actually very high as could be expected, but the city was spared from much of the pollen because of the upward air currents of warm air.

In order to visualize the effect of temperature on the fall-out of microscopic particles, a model "city" was built and Lycopodium spores were scattered above it. The powder then resembled a cloud that settled slowly and unevenly upon the miniature "buildings" and "lawns." The city was then warmed slightly to a temperature above that of the air and the experiment was repeated. This time the clouds over the city

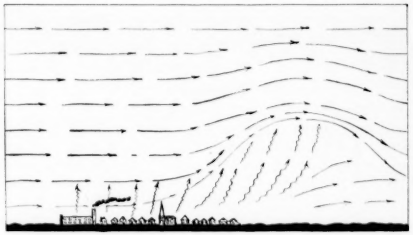

Fig. 2.—Drawing showing that rising currents of warm air over the city prevent much of the fall-out of pollens and molds. They have their greatest effect on the leeward side of the city.

billowed perceptibly but kept their distance from the ground and were finally dispersed over the rural areas. These observations have been recorded on motion-picture film.

Comment

Pollen and mold counts taken over and around a city indicate significant variations. The count is greatest on the windward side and least on the leeward side. These differences are ascribed to the temperature differences between the city and the country and can be explained by the effect of rising currents of warmer air over the city, which have their greatest effect on the leeward side.

The relationship of these findings to the fall-out of radioactive particles is obvious. Except for the danger of an atomic blast, a city should be safer from atomic fall-out than the surrounding country. Furthermore, the naturally higher temperature of a city may be increased by artificial means. Even in warm weather, houses could be heated, windows opened on the leeward side, and street lights turned on. Even an isolated village or a single residence may derive some protection by lighting fires on the windward sides. Practical application of our findings may prevent the hysterical exodus from a city to a more dangerous rural area in the event of an atomic attack.

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MUCORMYCOSIS—A NEW DISEASE?

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• *Mucormycosis is a disease caused by certain fungi, especially Rhizopus, that are common contaminants of laboratory cultures and not ordinarily pathogenic. The fungi enter the nose, and in susceptible patients they produce sinusitis and orbital cellulitis, penetrate arteries to produce thrombosis of the ophthalmic and internal carotid arteries, and later invade veins and lymphatics. There are ocular, cerebral, pulmonary, intestinal, and disseminated forms of the disease. The orbital involvement is illustrated in two case histories. One patient died in coma after the invasion of the meninges and brain; the other recovered but had residual blindness in one eye. There is reason to suspect that uncontrolled diabetes, leukemia, antileukemic drugs, some antibiotics, and cortisone render a patient susceptible to the invasion. Diagnosis depends on recognition of the fungus in specimens of tissue or of body fluids. Treatment consists in controlling the diabetes if present and discontinuing the use of the suspected drugs.*

Mucormycosis is a new disease in the United States. A report of the cerebral form appeared in 1943[1] and one on the pulmonary form in 1948,[2] and, although fatal cases have increased in frequency,[3] Harris[4] published the first account of a clinical case with recovery in 1955. The disease occurs more frequently than is realized, and without biopsy or autopsy diagnosis might be overlooked. Therefore, physicians will wish to know of this fungus infection and of the circumstances under which it develops.

Cases have been observed in all parts of the United States, Canada, and England, and the disease is probably world-wide. It is usually encountered as a complication of other diseases, of which diabetes mellitus and leukemia are the commonest, but multiple myeloma, fatal burns, and cirrhosis are other antecedent conditions. Cortisone, corticotropin, (ACTH), antileukemic chemical agents, and antibiotics may be other predisposing factors. The improvement in the control of bacterial diseases by the use of antibiotics may explain why mucormycosis is more frequent. Diabetics who formerly developed micrococcic (staphylococcic) infections may now contract this new fungus infection.

Mucormycosis is caused by fungi that are common in nature, common as laboratory contaminants, and not usually considered to be pathogens. The spread of the fungus is unique among micro-organisms, for it has great affinity for arteries. It penetrates the tough muscular walls, grows within the lumina, and stimulates purulent arteritis or thrombosis. Later, it invades veins and lymphatics. As a result of the vascular occlusions, infarcts form and are characteristic of the disease. Thus the lesions are a combination of infarcts and inflammatory response toward the invading fungus. Furthermore, this fungus infection is notable among mycoses because it is acute rather than chronic. The disease takes cerebral and pulmonary forms and, rarely, intestinal, purely ocular,[5] and disseminated forms.

Cerebral Mucormycosis

A recent fatal case[6] illustrates this form of the disease.

A white male, aged 62, had had a portacaval shunt operation performed two years ante mortem and had been relieved of all symptoms of cirrhosis. Two weeks before death he developed fever and orbital pain. Daily penicillin therapy produced no improvement. Three days before death he became comatose. Study at the Veterans Administration Hospital in Durham, N. C., in March, 1956, revealed xanthochromic, bloody spinal fluid and occlusion of the left internal carotid artery. The left eye became proptotic and chemotic.

At autopsy there was hemorrhagic proptosis of the left eye. Thrombotic occlusion of the left internal carotid artery was demonstrated. The left sphenoid sinus contained bloody pus, and the mucosa of this air sinus and of the left ethmoid sinus was congested. There was moderate diffuse subarachnoid hemorrhage, and the brain was softer than normal.

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Chairman's address, read before the Section on Pathology and Physiology at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

Microscopically, branching, nonseptate hyphae were demonstrated in the mucosa of the air sinuses, often surrounded by pus cells and often within vessels. Enormous numbers of fungus filaments grew in the wall of the internal carotid artery and filled its lumen. At one point this vessel had leaked blood, due to the fungus infiltration of the wall, and had produced the subarachnoid hemorrhage. Fungi were present in the vessels of the leptomeninges, free in the meninges and in all parts of the brain, with acute meningoencephalitis.

Thirteen fatal cases of this sort have been reported since 1943.[7] The patients have been of all ages, from 5 months to 65 years, and sex and race have seemed to be irrelevant. Ten of the 13 presented orbital and 4 paranasal features, while carotid artery thrombosis was frequent. In seven there was diabetes mellitus.

The fungus appears to enter by the nose and to produce sinusitis and orbital cellulitis, with thrombosis of the ophthalmic and internal carotid arteries. The fungus permeates the fat, nerves, perineural lymphatics, and veins of the orbit. In several cases the fungus produced brawny red induration of the cheek, which apparently represented infarction. Cerebral softening is also in part the result of infarction, though organisms extend deeply into the brain and produce a mycotic encephalitis.

Mucormycosis of the paranasal sinuses and orbit may develop without cerebral lesions, and with clinical recovery of the patient.[4] For example, the following case is cited.

In 1954 a Negro girl, aged 12, entered Duke Hospital in diabetic acidosis with a bulging left eye (fig. 1), ophthalmoplegia and loss of vision of this eye, loss of sensation of the left cheek, and an ulcer of the roof of the mouth. The roentgenogram showed increased density of the left ethmoid and maxillary air sinuses as contrasted with the right (fig. 1). A biopsy specimen from the palatal ulcer showed the characteristic broad hyphae of mucormycosis, growing in vessels and lymphatics as well as diffusely in the tissues. Rhizopus arrhizus was cultured from the ulcer.

The child's diabetes was carefully regulated with insulin; desensitization of the child to antigens of the culture was accomplished; and iodides were given. On this regimen the child re-

covered and was alive and well more than a year later, with diabetes, residual blindness of the affected eye, and sensory loss of the left side of the face.

A second case of this type, in an adult with diabetic acidosis, presented with symptoms of severe left ethmoidal sinusitis.[6] Great swelling of the left eye was present. The diagnosis of mucormycosis was made by

Fig. 1.—Mucormycosis: *left*, orbital swelling of left eye; *right*, unilateral sinusitis.

microscopic study of the excised lining of the sinus, and Rhizopus was cultured from the operative incision. Careful regulation of the diabetes resulted in recovery of the patient.

Pulmonary Mucormycosis

Pulmonary mucormycosis [3] is of two types, primary and hematogenous. Primary pulmonary mucormycosis develops from fungus growth in the bronchi. Organisms penetrate the walls of bronchi and infect the

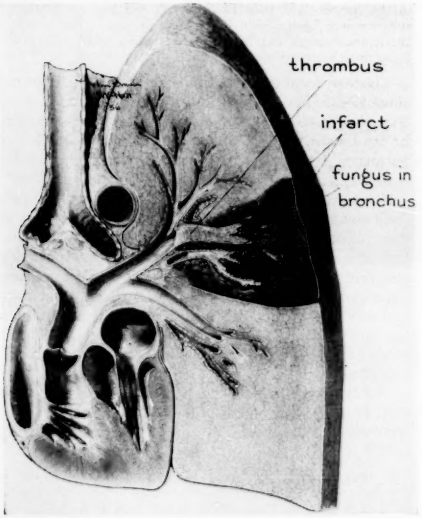

Fig. 2.—Mucormycosis of lung: fungus in bronchus; thrombus in branch of pulmonary artery; pulmonary infarct.

hilar tissues. The fungus then invades the pulmonary artery and vein and causes thrombosis, which results in pulmonary infarction (fig. 2). To a less extent pulmonary mucormycosis is a lobular pneumonia, representing inflammatory response to the presence of the fungus.

The onset may be sudden, with the production of severe pain in the chest, a pleural friction rub, and bloody sputum. This coincides with the development of the infarct. In other cases the consolidation may form insidiously. Fever and leukocytosis are present. In one case, for example, the white blood cell count was 23,550 per cubic millimeter, with 94% neutrophils. Roentgenograms reveal pulmonary consolidation. The duration of the mycosis in the 10 reported cases, all fatal, has varied from 3 to 30 days. Pulmonary mucormycosis appeared to be the main cause of death in six and in four, an incidental finding at autopsy. It is characteristic that the lesions of pulmonary mucormycosis do not respond to antibacterial agents.

Other Forms of Mucormycosis

Intestinal mucormycosis presents as hemorrhagic segments in the ileum or large intestine (fig. 3). In two cases to be reported elsewhere,[8] the largest hemorrhagic and ulcerative lesions were in the terminal section of the ileum. Disseminated mucormycosis, with lesions in many organs, has been reported.[3]

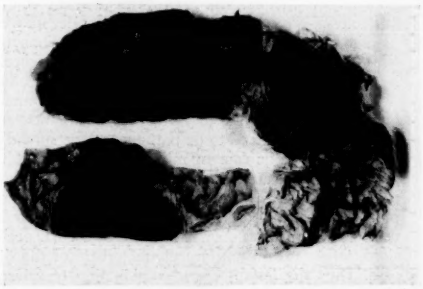

Fig. 3.—Mucormycosis of intestine: smaller segment presents hemorrhagic ulcerative lesion of ileum, larger segment shows hemorrhagic ileum (left), with ileocecal valve to right and large intestine below.

Comment

The Organism.—Rhizopus, rather than Mucor, appears to be the usual cause of human mucormycosis. Rhizopus grows rapidly and is characterized by rhizoids in microscopic structure (fig. 4). The feature common to mucormycosis is the presence of broad (4 to 20 μ thick), branching, predominantly nonseptate hyphae in the lesions, with the characteristic invasion of arteries and veins, producing thrombosis and infarction (fig. 5).

Predisposing Factors.—What factors cause this usually harmless fungus to assume pathogenicity? In diabetics the important feature is not diabetes alone, but rather the presence of uncontrolled and acidotic diabetes.[9] Rabbits and mice with chronic alloxan diabetes are as resistant as normal control animals to experimental Rhizopus infection.[10] However, in the acutely toxic state of alloxan diabetes fulminating mucormycosis can be produced.[11] There is evidence from animal experiments that cortisone favors dissemination of the organism.[12] The use of bacterial antibiotics probably favors the development of the infection, but this has not been proved experimentally.

Diagnosis.—The diagnosis of mucormycosis has been made by examination of tissue specimens taken at biopsy or autopsy. A diagnosis should be possible by examination of sputum, spinal fluid, or exudate. Culture of Rhizopus is corroborative. Since Rhizopus is a common contaminant, the recovery of this organism in culture is not in itself diagnostic.

Treatment.—Treatment by desensitization of the patient to an autogenous vaccine, followed by iodine therapy, may be used. Since effective chemotherapeutic agents against Rhizopus are not available, treatment depends on the control of the predisposing disease. Regulation of diabetes is indicated. The use of cortisone, corticotropin, and bacterial antibiotics should be discontinued or reevaluated.

Summary

Mucormycosis is a new disease in the United States, its occurrence being reported with increasing frequency, probably due to the use of antibiotics, which reduce the number of bacterial infections but permit fungus invasion. Cortisone and antileukemic drugs may favor the development of this mycosis. Predisposing diseases, especially diabetes mellitus or leukemia, are the common forerunners of mucormycosis.

The usual cause of the disease is an ubiquitous laboratory contaminant, Rhizopus. In cerebral mucormycosis, this fungus enters the nose and leads to sinusitis, orbital cellulitis, meningoencephalitis, and thrombosis of the internal carotid artery. In pulmonary mucormycosis the fungus invades bronchi and produces thromboses of pulmonary vessels, pulmonary infarcts, and lobular pneumonia. Ocular, intestinal, and disseminated forms occur.

The duration of the disease is relatively short in fatal cases, usually varying from one day to one month. Clinical recovery of patients with sinusitis and orbital cellulitis has been reported.

The diagnosis rests upon demonstration of the fungus in the lesions. Treatment is dependent largely upon the treatment of the underlying predisposing condition.

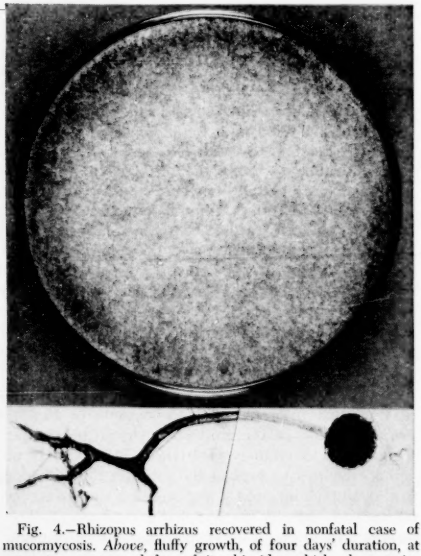

Fig. 4.—Rhizopus arrhizus recovered in nonfatal case of mucormycosis. *Above*, fluffy growth, of four days' duration, at room temperature; *below, left*, rhizoids, which characterize Rhizopus; *below, right*, sporangium containing minute spores.

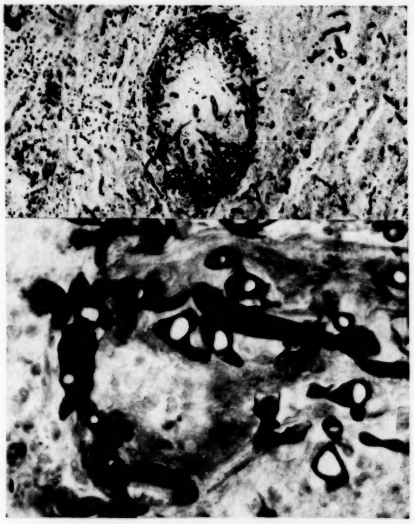

Fig. 5.—*Above*, tissue of hilus of lung with fungus hyphae in and around small vein in case of pulmonary mucormycosis (hematoxylin and eosin stain). *Below*, hyphae of fungus stained intensely black, in wall and lumen of thrombosed venule of brain, in case of cerebral mucormycosis (silver stain).

Veterans Administration Hospital.

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Figure 3 appeared previously in Baker, Bassert, and Farrington.[8]

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PRIMARY TUMORS OF THE URETER

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• *The possibility of a ureteral tumor should be considered in any case of unilateral hydronephrosis in which the cause is not evident. In 20 cases of primary neoplasms of the ureter, 14 diagnosed as carcinoma and 6 as papilloma, 17 of the tumors were located in the lower half of the ureter. Hematuria was present microscopically in 70% (14) of the cases, and in almost all of these cases the urine was grossly bloody. The best treatment for this type of tumor, assuming a normal kidney on the opposite side, is complete nephroureterectomy with segmental bladder resection.*

While primary tumors of the ureter are still considered as rare, they are without doubt of more frequent occurrence than they were considered to be previous to 1940. The present paper is based on 20 cases of primary ureteral tumor, 6 classed as benign and 14 as malignant, some of which were my own and some of which were those of my colleagues. Sixteen cases were seen on the urologic service at the New York Hospital and four cases were seen during a 10-month period in 1952 on my urologic service at the Hackensack (N. J.) Hospital, an institution of about 375 beds. The 16 cases at the New York Hospital included all cases of primary ureteral tumors seen from 1932 to the present. In selecting these 16 cases, I excluded 20 cases as representing secondary ureteral tumors. In case of doubt, an attempt was made to err on the side of certainty that the tumor was actually primary in the ureter.

In this presentation, I will not attempt to present an exhaustive review of the literature, but a few remarks on history and incidence may be in order. Most authors credit Rayer with having described the first case of primary ureteral tumor in 1842. However, it was in 1878 that Wising and Blix [1] reported the first case of primary ureteral carcinoma, with diagnosis based upon microscopic studies of sections from the tumor. Foord and Ferrier [2] report only eight cases recorded in the literature by 1900, and in these all diagnoses were based on autopsy examinations. In 1939 they reported a total of 139 cases in the world's literature and added 6 new cases. It was in 1902 that Albarran [3] made the first correct preoperative diagnosis. Savignac [4] reported 333 cases of primary ureteral carcinoma to October, 1955, of which 137 cases had been reported in the previous five years. In 1943 Scott [5] gave an excellent review of the world's literature on this subject up to that date.

As to incidence, Renner [6] found three cases in 13,854 autopsies at the Vienna Pathological Institute. Colston, in 1934, reported two cases in 22,000 admissions to the urologic service of Johns Hopkins Hospital. Jaffe and Mendillo [7] found two cases in 90,000 routine admissions to Grace Hospital. Gilbert reported only one case in 22,810 autopsies at Bellevue Hospital, 1904 to 1935. Soloway [8] found four cases in 26,410 autopsies at Cook County Hospital in Chicago (1930 to 1951).

No extensive discussion of etiology will be attempted in this paper. The causes of tumors of the ureteral epithelium are no doubt the same as the causes of tumors of "urothelium" elsewhere in the urinary tract. Although these causes are unknown, the following possible causative factors have been advanced: (1) local irritants, (2) embryonal cell rests, (3) parasites, (4) leukoplakia, (5) endogenous chemicals, and (6) exogenous chemicals. The contention that urinary epithelial hyperplasia is due to local irritation from chronic infection or noxious agents in the body fluids is in disagreement with Von Brunn's theory of "cell nests" as the site of origin. Fagerstrom [9] holds that epithelial buds and crypts are bizarre manifestations of epithelial hyperplasia. It is reasonable that all primary tumors of the urothelium should be grouped together as to etiology. The three most widely accepted theories to explain the multiplicity of tumors in the urothelium are (1) implantation by surface extension, (2) spread via lymphatic channels, and (3) multicentric origin. There is considerable clinical support for the theory of multicentric origin. Willis [10] states, "when a carcinogenic factor is applied to tissue, it is not applied to a single focus but to a more or less extensive field of the tissue. Visible tumor formation usually commences at one or more small foci in that field, but the neoplastic change extends from these to the other parts of the field."

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Read before the Section on Urology at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

History of Cases

Instead of presenting a detailed history of each of the 20 cases of primary ureteral tumor included in this study, I have listed the essential data in the table.

Age.—The age of patients varied from 45 to 87 years, the decade of highest incidence being the sixth. There were 15 males and 5 females. In 235 cases Scott [11] found that the males outnumbered the females two to one.

clots. Pain occurred in 9 of the 20 cases. In one instance (case 5) it was due to metastatic involvement of the left hip, although the primary ureteral tumor was classed by the pathologist as papilloma.

A palpable mass was present in four cases, in each instance due to a different cause. In one case the mass palpated was a large metastasis in the left ilium; in one the mass was a hydronephrotic kidney; in a third, the ureteral tumor itself was palpable abdominally; and in one case the tumor was palpated rectally and

Data on Twenty Cases of Primary Ureteral Tumor

Case No.	Sex and Age, Yr.	Diagnosis Made Preoperatively	Papanicolaou Test	Treatment: Nephrectomy, Partial Ureterectomy	Treatment: Complete Nephroureterectomy, Partial Cystectomy	Treatment: Irradiation or Other Treatment	Pathological Diagnosis	Living, Mo. Postoperatively	Died, Mo. Postoperatively	Comment
1	F, 70	+	2		+		Papilloma	12		No evidence of neoplasm
2	M, 58	+—Tumor or stone				Partial ureterectomy; nephrectomy later	Papilloma	120		No evidence of neoplasm
3	M, 55	+	1		+		Papilloma	14		Recurred in prostatic urethra; no evidence of neoplasm
4	M, 60	+			+		Papilloma		72	Died of carcinoma of lung 2 yr. after operation for primary carcinoma of lung
5	F, 60	+		+			Papilloma; metastases in ilium		12	With bony metastases
6	F, 45	+	2,3,4	+ FZ,* benign			Papillary carcinoma	92		Recent cystoscopy negative
7	M, 51	—			+ 2 stages		Papillary carcinoma		44	With carcinoma
8	M, 45	—			+ 2 stages		Papillary carcinoma		35	With carcinoma
9	M, 63	+			+		Papillary carcinoma	30		No evidence of neoplasm
10	M, 69	—				Exploration of ureteral stump	Nonpapillary carcinoma		7 days after exploration	Nephrectomy 9 mo. previously for tuberculosis
11	F, 59	+	3,4,5		Single incision	+ 4,454 r	Nonpapillary carcinoma; positive extension to iliac node	24		Recent cystoscopy negative
12	M, 52	+—		+ Pyonephrosis		+ 6,000 r	Nonpapillary carcinoma		16	With carcinoma; had small stone also
13	M, 57	+—					Papilloma	102		Spontaneous rupture of kidney; recent examination negative
14	M, 45	—				Tumor (large) excised with bladder cuff; kidney left + 6,000 r	Nonpapillary carcinoma		16	With recurrence
15	M, 50	—				Perineal Partial excision + 5,422 r	Nonpapillary carcinoma		2	With evidence of neoplasm
16	M, 72	+		+		+ 5,200 r	Nonpapillary carcinoma		14	With recurrence
17	F, 87	+		+			Papillary carcinoma		12	No evidence of recurrence
18	M, 68	+			+		Papillary carcinoma	60		Recent cystoscopy negative
19	M, 47	+		+ Segmental resection 9 mo. later			Papillary carcinoma		46	Extensive metastases
20	M, 80	+		Diagnosed 6 wk. ante mortem; then too ill, due to uremia & nephritis for operation			Papillary carcinoma			Autopsy done

* FZ=frozen section.

Location.—Seventeen tumors were located in the lower half of the ureter and three in the upper half. The sides were evenly divided, 10 right and 10 left. There were no cases of bilateral tumors. Scott found 2 cases of bilateral tumors in a total of 240 cases.

Signs and Symptoms.—Hematuria was present microscopically in 14 cases (70%). In some cases hematuria was evident only microscopically, but in almost all cases the urine was practically pure blood. In many cases the hematuria was painless, but in some instances there was colicky pain due to the passage of

diagnosed as a tumor of the seminal vesicle. A greater or lesser degree of hydronephrosis was present in 18 cases (90%). Other symptoms occurring were frequency of urination, anorexia, nausea, loss of weight, weakness, and, in some cases of infection, fever.

Diagnosis.—In most previously reported series of ureteral tumors, a correct preoperative diagnosis has been made in about 50% of cases. In this series of 20 cases, 12 diagnoses were correctly made preoperatively (one ante mortem), and 3 patients were given a diagnosis of possible ureteral tumor. In five cases the

diagnosis was missed. In four cases the tumor was evident at the ureteral orifice upon cystoscopic examination.

A Papanicolaou test was done one or more times in each of four cases. In one case of papilloma it was class 1, and in another, class 2, as one would expect, judging by results in diagnoses of vesical papillomas.

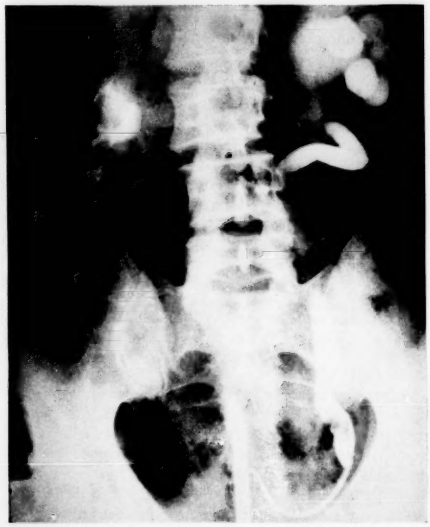

Fig. 1 (case 2).—Filling defect in lower part of left ureter; transitional cell papilloma; patient alive and well 10 years after operation.

In case 6 (papillary carcinoma) the Papanicolaou test was class 2, 3, or 4 on different tests. In case 11 (nonpapillary carcinoma) the Papanicolaou test on different trials was class 3, 4, or 5. One can say that the Papanicolaou test is probably of value in these cases. Such a study of the urine from the suspected side should be done if possible.

Plain x-ray examination may be of value in suspected cases in demonstrating metastatic involvement of the lungs or bones. In this series in one case (12), nonpapillary carcinoma was associated with renal calculus. Excretory urography may show obstruction of a ureter and kidney or nonfunction of a kidney. In some cases a ureteral filling defect may be demonstrated, but usually a retrograde ureterogram is required to do this. If the patient has had previous x-ray examination, it is important to secure the previous films for comparison with the present ones. Cystoscopy may show a papillary growth protruding from the ureteral orifice, or, occasionally, a small projection of the growth may be seen only when the orifice is discharging urine. It may also reveal a bloody efflux from the affected side.

If excretory urography has demonstrated obstruction or nonfunction on one side, then retrograde pyelography should be performed. Sometimes a catheter cannot be passed up the suspected ureter or the ureterogram obtained in this manner may not be satisfactory. In this case a more satisfactory ureterogram can usually be obtained by means of the Braasch or Woodruff bulb. If a filling defect is seen on excretory urography, this should be confirmed by the retrograde ureterogram. The possibility of a ureteral tumor should be considered in any case of unilateral hydronephrosis, the cause of which is not evident. Occasionally, the presence of a ureteral calculus in addition to a tumor may complicate the diagnostic picture. The use of a wax bulb may be helpful in such a case.

A tumor in the intramural portion of the ureter but not appearing at the orifice may cause a bulge in the ureteral ridge or, if it is quite small, may give the ureterographic picture of stricture only. Sometimes, as in case 18, one secures bloody urine when the ureteral catheter is in the lower part of the ureter but, when the catheter is inserted higher, above the tumor, perfectly clear urine is obtained. This situation makes the diagnosis almost certain.

The use of a Johnson basket to secure tissue for biopsy has been suggested, but I would not recommend it. A better method is to secure a biopsy specimen by means of a ureteral catheter by suction.

The ureteral filling defect caused by tumor may assume various forms, depending upon the size, shape, and consistency of the tumor (fig. 1, 2, 3, 4, and 5). It may appear like a stricture or it may be ovoid or goblet-shaped, or it may present a very irregular, moth-eaten appearance.

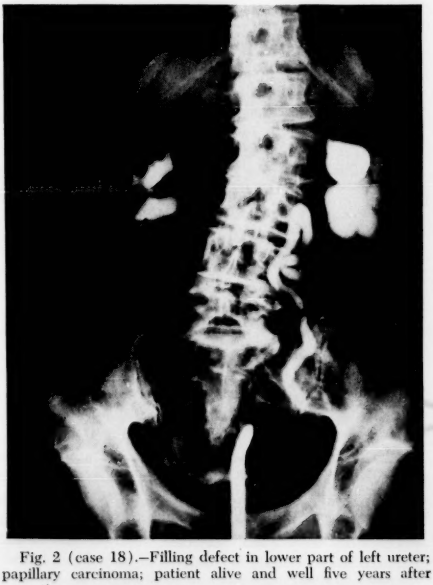

Fig. 2 (case 18).—Filling defect in lower part of left ureter; papillary carcinoma; patient alive and well five years after operation.

Pathology.—Of the 20 cases, 6 were classed as papilloma and 14 as carcinoma. Of the 14 carcinomas, 8 were papillary and 6 nonpapillary. The carcinomas could be further subdivided, but I believe that this simple classification is sufficient for this discussion. It should be noted that some authors classify ureteral papillomas as grade 1 carcinoma. Certainly they should be considered as potentially malignant, just as vesical papillomas are thus considered.

I have not included in this series one unusual case indexed at the New York Hospital as primary ureteral carcinoma. This was a 41-year-old man who entered the hospital Nov. 18, 1947. A diagnosis of tumor of the right ureter was made, and at operation a very large mass was found surrounding the lower portion of the right ureter. Some biopsy specimens (six) were taken, and one of these showed carcinoma of the ureter of epidermoid type, but the other specimens did not show carcinoma. This exploration was followed by irradiation, and the family was told that the patient would die soon. However, he began to improve after a few months and is still alive eight years later. On Jan. 5, 1956, excretory urography showed a normal upper urinary tract.

Treatment.—Many types of operations have been used in these cases. Scott[5] listed 52 types of operations in 206 primary ureteral carcinomas. Failure to make a correct preoperative diagnosis in almost half of the cases probably accounted in large degree for the great variety of operative procedures. In general, one can say that the best treatment for primary ureteral tumors, assuming a normal kidney on the opposite side, is complete nephroureterectomy, with excision of a bladder cuff in one or two stages (one, if the patient is in reasonably good condition). In freeing the ureter, the fatty tissue adjacent to it should be included. In suitable cases the best procedure, assuming the tumor is in the lower part of the ureter, is to expose the primary lesion through a Gibson type of incision and carefully separate the ureter down to the bladder. A cuff of bladder about 2 cm. in radius around the ureterovesical orifice is then resected. As advocated by Cook,[12] this portion of the ureter and the attached bladder wall is then covered by a Penrose drain to prevent contamination. This incision is then closed and the patient is placed in position for a lumbar incision. The kidney is then removed, along with the attached ureter and bladder cuff.

Fig. 3 (case 19).—Extensive filling defect in lower part of right ureter; patient died 46 months after operation with extensive metastases.

Figure 4 (case 17).—Eighty-seven-year-old man; filling defect in right ureter; died 12 months after operation without evidence of recurrence.

In a thin patient one can do the entire procedure satisfactorily through a single, extended lumbar incision, but, in general, two incisions are preferable. Two stages may be used if the patient's general condition is poor. In two cases in this series a two-stage procedure was done because, at the time of nephrectomy, the presence of the ureteral tumor had not been detected. In one of these cases the kidney had been removed five months previously because of a very large hemorrhagic cyst.

The types of operations performed in this series were as follows: nephroureterectomy, with segmental bladder resection, six; nephroureterectomy, without bladder cuff, six; nephrectomy, later ureterectomy with bladder cuff (correct diagnosis not made before nephrectomy) two; nephrectomy and partial ureterectomy (pyonephrosis; diagnosis of ureteral tumor not known preoperatively) one; partial ureterectomy with

bladder cuff (kidney not removed because of patient's general condition) one; partial ureterectomy with bladder cuff, ureter put on skin (15 months later, nephroureterectomy) one; exploration of mass in left loin with biopsy only, one; and perineal exploration with partial

Fig. 5 (case 20).—Eighty-year-old woman; stricture at lower end of right ureter; diagnosed ante mortem, but not operated on because of uremia and nephritis; autopsy performed—papillary carcinoma.

removal, one. In one case, correct diagnosis was made ante mortem, but no operation was done because of uremia and nephritis.

A brief summary of one of my cases follows.

Case 18.—A 68-year-old male entered Hackensack Hospital April 24, 1951, with a history of gross hematuria and dull pain on the left side of two weeks' duration. History was irrelevant. Cystoscopic examination revealed blood coming from the left ureteral orifice. When a catheter was passed up the left ureter, clean urine was obtained from the upper part of the ureter and the renal pelvis. As indicated in figure 2, the left pyelogram showed a grade 3 hydronephrosis and hydroureter on the left, with a definite irregular filling defect in the lower part of the left ureter. The right pyelogram was within normal limits, and the chest plate and x-rays of long bones were normal. A diagnosis of primary tumor of the lower part of the left ureter was made, and on April 26, 1951, a nephroureterectomy on the left, with segmental resection of the bladder, was performed (two incisions were used). Pathological diagnosis was papillary carcinoma of the ureter. There was no deep invasion of the ureteral musculature (fig. 6). The postoperative course was smooth, and he was discharged May 9, 1951. Since discharge, he has undergone cystoscopy periodically, and the last cystoscopy in January, 1956, showed no evidence of recurrence, almost five years after operation. A chest plate showed a definite, smoothly outlined enlargement on the right side of the cardiac shadow. The chest was explored Feb. 13, 1956, and a large, serous, pericardial cyst was excised. He is now 73 years of age and is enjoying good health.

Vest,[13] in an excellent article, has advocated conservative treatment in carefully selected cases, including some cases of benign papilloma. Any decision to use conservative surgery must, of course, be made with the utmost caution, taking into consideration all factors involved, including the functional status of both kidneys. If one uses all the safeguards and criteria mentioned by Vest, I believe conservative surgery is justifiable in an occasional instance of benign ureteral tumor.

Results

In this series there was no death after operative removal of a ureteral tumor; however, in case 10, death occurred seven days after surgical exploration and biopsy in a patient with an advanced ureteral carcinoma, who had had a nephrectomy for tuberculosis nine months previously. In case 20 no operation was performed, so there were 18 cases in which operative removal of the tumor was performed with no mortality. It was possible to secure follow-up data for all of these 18 patients.

Of six patients with benign papilloma, one (case 5), who had a large metastasis in the left ilium at the time of operation, died one year later with extensive metastases. The pathologist called the tumor benign

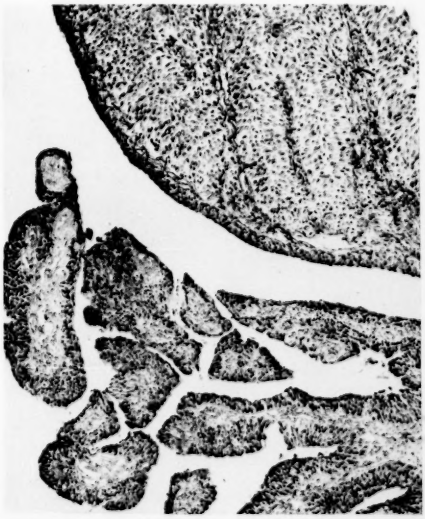

Fig. 6 (case 18).—Same case as figure 2; papillary, transitional cell carcinoma of ureter; photomicrograph showing tumor present at surface and invading submucosa.

because there was no invasion of the submucosa or muscularis. In case 4, the patient was well for four years when he developed carcinoma of the lung and had the right lung removed at Deaconess Hospital, Boston, by Dr. Overholt, who considered it a primary tumor of the lung. He died two years later, with recurrence of pulmonary carcinoma. There was no recur-

rence of tumor in the bladder at any time. The other four patients operated on for ureteral papilloma are alive and well at the following periods after operation: 12, 14, 102, and 120 months respectively.

Of the eight patients with papillary carcinoma, one had a correct diagnosis made six weeks before autopsy but was not operated on because of uremia and nephritis. One died a year after operation at 88 years of age without evidence of recurrence, while three others died 35, 44, and 46 months after operation, all with evidence of carcinoma. Three patients are still alive without demonstrable recurrence at postoperative periods of 30, 60, and 92 months respectively.

Of six cases of nonpapillary carcinoma, one patient, with an advanced neoplasm, had only an exploratory operation with biopsy and died seven days later. Four patients died with evidence of neoplasm 2, 14, 16, and 16 months after operation. One patient (case 11) who had a positive external iliac lymph node, is alive 24 months after operation without any signs of recurrence. She underwent cystoscopy Feb. 20, 1956, 22 months after operation. The Papanicolaou test in this case was positive, 4 and 5. This is a most unusual situation.

It is seen that those patients who died of recurrence or metastasis did so within four years. No patient surviving four or more years after operation has shown any subsequent evidence of recurrence. Postoperative irradiation was used in five cases. Its curative value is somewhat equivocal, but it appears to be of value in the relief of pain due to metastasis or recurrence.

Summary and Conclusions

Primary ureteral tumors are being discovered with increasing frequency, due to greater awareness and better diagnostic methods. Of 20 cases reported in this series, 6 were diagnosed as papilloma and 14 as carcinoma. All patients had a follow-up study.

In all patients with unilateral hydronephrosis without evident etiology, the possibility of primary ureteral tumor should be investigated by all available diagnostic methods, including retrograde ureterograms made with the Braasch or Woodruff bulb and Papanicolaou smears.

Surgical treatment should be instituted as early as possible and, in almost all cases, should consist of nephroureterectomy with segmental bladder resection. In an occasional case of "benign" tumor, some form of conservative treatment may be used, with observation of all the precautions outlined by Vest. Operative mortality should be very low. In this series the only death occurred seven days after an exploratory procedure for an extensive tumor in a ureteral stump.

The results of surgical treatment vary with the completeness of operation, the operability of the tumor, and the degree of malignancy involved. The result is generally favorable if the tumor has not penetrated the ureteral musculature deeply.

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Galvani's Twitching Frogs' Legs.—One of the most often quoted discoveries in which accident played a large part has to do with the origin and development of our knowledge of electrical phenomena. It is said that in the Galvani home in Bologna some frogs' legs suspended by copper wire from an iron balustrade were observed to twitch when blown by the wind against the iron. This observation led to many important experiments, including those of Volta on the production of electrical currents by contact of two dissimilar metals and thus to the invention of the electric battery. Such were the observations that led ultimately, directly or indirectly, to the invention of the telegraph, the telephone, radio broadcasting, and television. Such also was the origin from which our knowledge of animal electricity has been developed and has resulted in the electrocardiogram and the electroencephalogram. Oersted found by accident that an electric current in a wire can move a magnet, and later Faraday showed that a moving magnet can cause a current to appear in a wire. Thanks to such discoveries we have electric lights, refrigerators, sparks in motor cylinders, and many other devices that help to make life more pleasant but at times more dangerous. It is obvious that the twitching of Galvani's frogs' legs has had a tremendous influence on the history of mankind.—A. Blalock, M.D., The Nature of Discovery, *Annals of Surgery*, September, 1956.

CONSERVATION OF HEARING—FENESTRATION OR STAPES MOBILIZATION

Clair M. Kos, M.D., Iowa City

• *Hearing impairment caused by otosclerosis was treated by mobilization of the stapes in 400 cases. The prospect of benefits from the operation was found to depend largely on the category of otosclerotic hearing defect. The category marked by normal bone conduction with more than 35 db. of loss in air conduction was twice as likely to be helped by fenestration as by stapes mobilization. The category marked by normal bone conduction and less than 35 db. of loss in air conduction was more likely to be helped by stapes mobilization. A third category, patients with a bone-conduction loss of not below the level of 30 db. with an additional air-conduction loss of at least 20 to 25 db., likewise had more favorable results from stapes mobilization. Fenestration is still the cornerstone of modern otosurgical procedures, and it is still needed to improve the hearing of many patients in whom the stapes mobilization procedure fails. But stapes mobilization fulfills a need for patients whose hearing losses do not fall within the levels necessary for successful fenestration, and it sometimes restores serviceable hearing when the nature of the hearing loss precludes such improvement by the use of fenestration.*

Recent interest shown in the development of various techniques to mobilize the stapes for the correction of hearing loss due to otosclerosis is somewhat reminiscent of the controversial issues raised in connection with the introduction of one-stage fenestration. There was much skepticism and illogical criticism. Complications and risks were emphasized far beyond the limits of reasonable consideration. The main objection was based on the prediction that hearing improvement could not and would not last. Despite the discouraging speculation and the ofttimes heated discussions that took place, time, training, and talent eventually made fenestration a practical and valuable otosurgical procedure.

Stapes mobilization, which had been tried many years ago and abandoned and recently has been revived, is facing similar resistance.[1] Eventually the procedure must pass the tests that time, training, and talent will provide. With the protection provided by the use of antibiotics and the use of cleverly contrived instruments, improved magnification, and more intense illumination, as well as other advantages that did not exist during its early history, the stapes-mobilization operation shows some promise of becoming a valuable addition to the surgical repertoire of the otologist.[2]

Contrary to the spreading hope and belief, this surgical procedure, while less complicated and less extensive than fenestration, is not simple or easy. This is not an operation to be performed by the casual or opportunistic surgeon. It is safe in the hands of those who have devoted considerable time to the acquisition of skills required in surgery of the temporal bone and of fenestration techniques, but it is not without potential damaging effects. Anyone who attempts stapedial mobilization should possess the ability to carry out fenestration if it is indicated.

It is difficult to compare these two operations because of the diverse circumstances in which they may be used. These operations have little in common except that they provide the possibility of hearing improvement in patients with hearing loss due to otosclerosis. The applications of and the indications for the two operations overlap somewhat, but one is not a substitute for the other. Rather it is better to consider mobilization of the stapes as a preliminary or complementary procedure to fenestration in the management of clinical otosclerosis. Fenestration is limited in use to a rather select range of suitability, whereas the range of selection for stapedial mobilization extends to that larger group of patients for whom fenestration would be only doubtfully successful or an unquestionable failure.

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Read before the Section on Laryngology, Otology, and Rhinology at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

The results of fenestration can be predicted with a rather high degree of accuracy, but the results of stapes mobilization cannot be foretold with such confidence.[3] There is nothing about the examination of the patient that is of prognostic value or that can measure the extent and magnitude of the otosclerotic process, the resistance of the fixed foot plate to mobilization, or the probability of reducing the ankylosis.

If the hearing loss meets the requirements of suitability, fenestration can be done successfully after stapes mobilization has proved ineffective. Some techniques for stapes mobilization permit fenestration to be done at almost any time after the attempted mobilization. Other techniques require a waiting period of from 6 to 12 months.

Comparison of Fenestration and Mobilization Techniques and After-effects

The methods in the two operations differ greatly. Fenestration, which is comprised of three parts—performance of mastoidectomy, creation of the tympanomeatal membrane, and creation of the fenestra—bypasses the ossicular chain and the tympanovestibular junction to create a new avenue for sound near the ampullar end of the horizontal semicircular canal.[4] Mobilization of the stapes involves making a small peritympanic incision, exposing the lenticulocapitular joint, and applying suitable instruments on the head, neck, crura, or foot plate of the stapes.[5] The operation preserves and utilizes the ossicular chain to restore auditory function as nearly as possible without changing the structure of the external or middle ear.

Fenestration requires hospitalization for from 7 to 10 days, the use of general anesthesia, preoperative and postoperative preparation and care, and restrictions of diet. Stapes mobilization requires only one day of hospitalization, the use of local anesthesia, no preoperative or postoperative preparation and care, and no change in the patient's dietary habits or preferences. The operating time for fenestration is usually one and one-half to two and one-half hours. Stapes mobilization ordinarily requires 20 to 45 minutes. Vertigo, nausea, and vomiting are frequent aftereffects of fenestration, while none of these reactions follow stapedial mobilization. The certain knowledge of hearing improvement resulting from fenestration is delayed for two to three weeks postoperatively, while hearing improvement, with rare exceptions, is an immediate result of stapes mobilization. After fenestration, the wound requires treatment at varying intervals for weeks or months and, thereafter, at least annually. The operative site of the mobilization procedure does not require postoperative treatment.

Complications

Complications after either fenestration or stapedial mobilization are very rare. Hearing may become worse as the result of either procedure, but complete loss of residual hearing is more likely to occur after fenestration, due to the additional hazard involved in exposing the labyrinth to possible injury and inflammation.

Injury of the facial nerve may occur in the performance of fenestration, and, although such accidents are possible in operations for stapedial mobilization, this kind of injury is usually a sign of the surgeon's incompetence or carelessness. Perforation of the tympanic membrane is a potential complication in fenestration or operation for mobilization of the stapes unless the surgeon exercises reasonable skill and caution. Should a perforation be produced, a diaphragm of tissue paper or compressed absorbable gelatin sponge may be applied to seal the defect as it heals. It is possible that otitis media with its varied associated complications may result from operation for stapes mobilization unless adequate prophylactic therapy with antibiotics is given. Despite this protective measure, excessive surgical trauma may invite the development of resistant infection as it may with any surgical procedure.

The operation for mobilization of the stapes requires an intimate knowledge of the minute anatomic details of the ossicular chain in order to avoid incudostapedial dislocation, avulsion of the stapes, or fracture of the stapedial crura, which too frequently occurs. Fracture of the stapedial crura is not serious, but such an occurrence results in a loss of leverage against the foot plate and prevents further efforts at mobilization. These considerations are not of essential importance in fenestration, as the purpose of the operation is not concerned with the preservation of the ossicular chain.

The peritympanic incision used in the stapes mobilization operation may be the source of worrisome postoperative bleeding, but this has been virtually eliminated by the sealing of the incisional wound with a strip of compressed absorbable gelatin sponge. Should the strip be ineffectively applied or should bleeding occur in spite of it, a tampon of cotton inserted into the external auditory canal serves as an effective hemostat. Any additional intervention post-operatively may cause contamination and ensuing infection.

In 400 operations for mobilization of the stapes performed at the Univertity of Iowa Medical Center, one case of labyrinthitis occurred, from which recovery was complete without loss of the postoperative improvement in hearing. There were three cases of otitis media without residual damage to the ear or hearing. Postoperative bleeding occurred in 12 instances, but no permanent residual damage affected the ears. Hearing was made worse in 10 ears by levels of from 10 to 15 db. No cases of permanent perforation have occurred, and the facial nerve has not been injured in any patient. Perverted sense of taste due to injury to the chorda tympani nerve has been noted by three patients.

Results of Four Hundred Operations

Otosclerosis affects hearing in varying degrees. Essentially, it causes a mechanical type of functional impairment. However, there is very frequently an associated neural degeneration. These features of hearing loss are reflected in the air-conduction and bone-conduction thresholds.

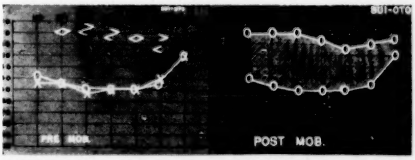

Fig. 1.—*Left*, audiogram showing level of hearing loss suitable for performance of fenestration because of normal bone conduction, upper line, with more than 35-db. loss in air conduction, lower line (category 1). In upper line < signifies bone conduction in left ear and > in right ear. In lower line X signifies level of air conduction in left ear and O in right ear. *Right*, upper line of audiogram, showing improvement in air conduction after stapes mobilization.

Consequently, four categories of otosclerotic hearing impairment may be recognized. 1. Normal bone conduction with more than 35-db. loss in air conduction. The magnitude of this hearing defect has been considered suitable for the performance of fenestration. Stapes mobilization can result in the restoration of practical and functional hearing in 30 to 40% of patients in this category. Fenestration will provide successful results in 60 to 80% of these patients (fig. 1). 2. Normal bone conduction with an air-conduction loss of 35 db. or less. Fenestration is not as likely to provide improvement in such cases as is stapes mobilization, which can result in appreciable improvement in about 50% of such patients (fig. 2). 3. Bone-conduction loss of not below the level of 30 db. with air-conduction loss of at least 20 to 25 db. This relationship provides for a gap between air and bone conduction of not less than 20 to 25 db. Stapes mobilization will

restore to about 30% of such patients a level of hearing better than 30 db., and about half of these patients will have improvement equal to the preoperative bone-conduction thresholds. Fenestration does not produce such favorable results in this group (fig. 3). 4. Bone-conduction loss greater than 30 db. with a minimum additional air-conduction loss of 20 to 25 db. Neither of the operations can restore practical and serviceable hearing in patients with such impairments, but the

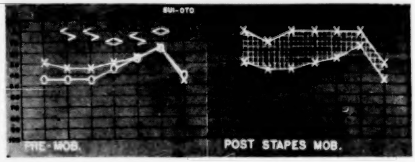

Fig. 2.—*Left*, audiogram showing less gap between normal bone conduction, upper line, and air-conduction loss of 35 db. or less, lower line (category 2), suggesting incomplete stapes fixation. *Right*, audiogram showing improvement in air conduction to essentially normal level of hearing after stapes mobilization.

hearing of about 50% may be improved 15 db. or more by stapes mobilization (fig. 4). Allegedly, this improvement permits them to wear hearing aids more effectively.

In only one of these categories can the results of fenestration and stapes mobilization be reasonably compared—the first category. In patients in this category fenestration is more than twice as successful as stapes mobilization, but fully one-third of them may not need fenestration if stapes mobilization is employed as a preliminary operation. In some of these patients the hearing may be restored to normal by mobilization of the stapes. Fenestration does not provide such spectacular improvement. Occasionally both operations may be employed to improve binaural hearing. In the remaining three categories fenestration cannot be equal in success to stapes mobilization. In these instances, stapes mobilization stands alone in effectiveness, and there is no logical reason for comparison.

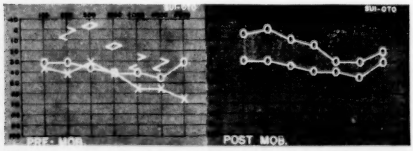

Fig. 3.—*Left*, audiogram showing hearing level in category 3: bone-conduction loss, upper line, of not below 30 db. and air-conduction loss of at least 20 to 25 db. *Right*, audiogram showing improvement in air conduction to practical and serviceable level after stapes mobilization.

Regression of hearing ability may follow either procedure. Regression occurs in about 10% of patients after stapes mobilization and in from 5 to 15% after fenestration. Most regressions after stapes mobilization occur within the first month postoperatively. Regressions after fenestration usually occur during the first 6 to 12 months postoperatively. An accurate and dependable comparison of regressions must await the results of considerably more study of mobilization.

If an appreciable improvement of hearing is obtained and regression then occurs, stapes mobilization may be used again with impunity. In such cases there is a 60% probability of restoring the original improvement of hearing. So far as is currently known, stapes mobilization may be repeated indefinitely at 6-to-12-month intervals.

Revisions of fenestration have a successful rate of about 20 to 25%. This is accompanied, however, by the serious hazard of severe damage to the inner ear. Fenestration revisions may also be repeated, but with progressively diminishing returns.

Conclusions

In the management of patients whose hearing impairments are due to otosclerosis, it is not a question of the superiority of one operation over the other. Fenestration is consistently effective within a limited group of patients, whereas stapes mobilization is helpful to a smaller percentage of these selected patients. The performance of fenestration is still necessary to improve the hearing of many patients in whom the

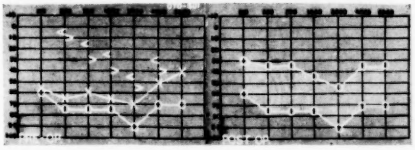

Fig. 4.—*Left*, audiogram showing bone-conduction loss below 30-db. level, upper line, with air-conduction loss of at least 20 to 25 db., lower line (category 4). Levels are not suitable for performance of fenestration. *Right*, audiogram showing improvement of air conduction after stapes mobilization to level equal to preoperative bone-conduction level.

mobilization procedure fails. Stapes mobilization fulfills a need for those patients whose hearing losses do not fall within the levels necessary for successful fenestration. The mobilization procedure may succeed in restoring practical and serviceable hearing when the nature of the hearing loss precludes such improvement by the use of fenestration.

Fenestration is the cornerstone of modern otosurgical procedures, and it is the basis for the thorough understanding of the various surgical procedures on the temporal bone. The operation has withstood more than 15 years of clinical and surgical cultivation. Stapes mobilization, by comparison, is but a product of the surgical dexterity gained from experience in modern temporal bone surgery. Its future retention in the pattern of surgical treatment of hearing impairment due to otosclerosis depends on results that will not be conclusive for several years.

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TREATMENT OF METABOLIC INSUFFICIENCY AND HYPOTHYROIDISM WITH SODIUM LIOTHYRONINE

PRELIMINARY REPORT

Elmore M. Fields, M.D., Hempstead, N. Y.

• *One hundred children, ranging in age from 1 to 18 years, of whom 40 had been given a diagnosis of metabolic insufficiency and 60 of hypothyroidism, were treated with the recently discovered hormone, sodium liothyronine. This product, believed to be the ultimately active thyroid hormone, appears to be three to five times as active as thyroxin, yet freer of side-effects. For the cases reported, the initial dose of liothyronine was 5 mcg. daily during the first week, increased to 15 mcg. by the third week depending on tolerance. No medicament was given during the fourth week, which was used as a cyclic rest period to allow for proper control of the individual's response while the therapeutic dosage level is being reached. By the third month a tolerance dose of 50 mcg. daily was usually attempted. The results in both diagnostic groups were good or excellent clinical improvement in over 90%.*

Metabolic insufficiency, while difficult to diagnose, especially in its subclinical form, may be the result of inefficient utilization of thyroid products at the cellular level rather than an inadequate supply of products from the thyroid gland. This diagnosis, as in hypothyroidism, is best determined by bone-age examination.

It is extremely important to recognize and treat thyroid deficiency in infants, children and adolescents, because a delay in treatment may determine the difference between future normal development and irreparable physical and mental retardation. The clinical symptoms of extreme thyroid deficiency in children with cretinism and myxedema are generally well recognized and unmistakable. Moreover, abnormally low basal metabolic rates and protein-bound iodine and radioactive iodine (I^{131})-uptake values can readily be interpreted as evidence of such thyroid dysfunction as severe hypothyroidism.

There is another disorder somewhat akin to, yet different from, hypothyroidism that often goes clinically masked, unrecognized, and untreated. This condition, which presents a relatively common clinical picture, has been termed metabolic insufficiency. In contrast to hypothyroidism, metabolic insufficiency produces only vague physical and emotional symptoms. It may exist in a patient who has normal protein-bound iodine and I^{131}-uptake values, and a normal or slightly subnormal basal metabolic rate.[1] Therefore, it has been postulated that this disorder may be caused by inefficient utilization of thyroid products at the cellular level rather than by an inadequate supply of products from the thyroid gland.[1b] For these reasons, the laboratory criteria can be too arbitrary, misleading, and nonspecific for the diagnosis of nonmyxedematous metabolic disorders, and the practitioner often must rely upon clinical criteria for detecting metabolic insufficiency.

Many symptoms of metabolic insufficiency resemble those of hypothyroidism, although the clinical picture differs in some respects. The most common clinical features of the former in children are irritability; fatigue; poor circulation, with coldness of the extremities; pains of the muscles and joints, with stiffness; dryness of the hair, with hypertrichosis and alopecia areata; hyperkeratosis of the skin, especially of the knees and elbows; small, wedge-shaped teeth, with delay in tooth eruption; constipation; allergic manifestations, such as colic, infantile eczema, and asthma; personality changes, such as willfulness, stubbornness, antagonism, lack of ability to concentrate, withdrawal, and immaturity; speech dysfunction; a delay in statural growth; poor eating habits; and moderate anemia. Various combinations of these symptoms may appear in the child with metabolic insufficiency. In some children, the symptoms and signs are subclinical and not easily recognized as evidence of metabolic insufficiency.

In order to confirm the diagnosis of hypothyroidism in children, I use roentgenographic bone-age determinations, because thyroid deficiency eventually and inevitably causes retardation in maturation of the carpal centers. (Epiphysial centers should not be used as a guide, since they are usually more retarded by pituitary dysfunction than by thyroid dysfunction.[2b]) If there is a delay of six months to one year in the

development of the carpal centers,[2c] the patient has a borderline thyroid deficiency. Any delay between one and two years indicates a moderately severe deficiency of thyroid, and a delay of more than two years indicates a severe deficiency. I have found that bone-age determinations are also valuable for diagnosing metabolic insufficiency in children. Retardation of carpal center development can be expected in this disorder as in hypothyroidism.

In the treatment of both metabolic insufficiency and hypothyroidism in children, it is evident that thyroid extract, thyroglobulin, and thyroxin often give satisfactory, sometimes dramatic, results. Yet these preparations are either ineffective or only partially effective for treating many children, especially those with metabolic insufficiency. Moreover, many children show manifestations of intolerance to these preparations by headaches, palpitations, hyperirritability, abdominal pain, restlessness at night, argumentativeness, crying episodes, or antisocial behavior. In such cases, therapy must be discontinued before adequate clinical improvements are obtained. However, a recently dis-

Response of Patients with Metabolic Insufficiency and Hypothyroidism to Treatment with Sodium Liothyronine

Diagnosis	Patients, No.	Results			
		Excellent	Good	Fair	Poor
Metabolic Insufficiency	40	22	15	3	...
Hypothyroidism					
Thyroid myxedema	6	5	1	...	...
Pituitary myxedema with secondary hypothyroidism	16	10	6	...	...
Mental retardation with primary hypothyroidism	4	2	2	...	...
Hypothyroidism with					
Allergic state	10	5	3	1	1
Growth deficiency	8	6	2	...	...
Diabetes insipidus	1	...	1	...	...
Achondroplasia	1	...	1	...	...
Amenorrhea	1	1	...	...	...
Mongolism	9	6	3	...	...
Cerebral palsy	4	...	3	1	...
Total	100	57	37	5	1

covered hormone, sodium liothyronine (L-triiodothyronine)[3] has shown promise of being more effective and freer of side-effects than thyroid extract, thyroglobulin, and thyroxin for treating metabolic insufficiency and hypothyroidism. Gross and Pitt-Rivers,[4] Lerman,[5] Starr,[6] and other investigators[7] have reported findings suggesting that this compound is the ultimately active thyroid hormone. It has been found to exert about three to five times the calorigenic and antigoitrogenic effect of thyroxin, it has a more rapid onset of action, and it has a quicker turnover rate in the body.[8] Since this compound became available for investigational use in July, 1955, I have tested its effects in 100 children. The aims of this study were to obtain a clinical impression of the efficacy of liothyronine in treating hypothyroidism and metabolic insufficiency in children and to compare the efficacy of liothyronine with that of thyroid extract, thyroglobulin, and thyroxin. Although it is still in progress, this study has produced results that seem to warrant a preliminary report on the clinical observations of the effects of liothyronine at this time.

Method of Study

One hundred children were selected for the study, 40 of whom were given a diagnosis of metabolic insufficiency. The other 60 had evidence of hypothyroidism and, in some cases, symptoms of other endocrinological disorders (see table).

The group with metabolic insufficiency consisted of 10 girls and 30 boys, all between 1 and 17 years of age. These children did not exhibit any of the classic features of cretinism or myxedema. Although they were normal in intelligence, many had poor school records, short attention spans, lack of ability to concentrate, and a "don't-care" attitude. They were thin, had poor appetites, and were somewhat constipated. They showed moderate symptoms of anxiety and restlessness. Fluoroscopic examinations showed that all of these children were retarded in bone development; the average retardation was about 18 months. Basal metabolic rates, determined in the older children, were significantly low, around –20 to –30%. Serum cholesterol levels averaged about 290 mg. per 100 cc. Protein-bound iodine levels, determined in 25 children, were normal, raging from 3.8 to 8.6 mg. in 100 cc. of serum.

In the group with hypothyroid disorders, there were 25 girls and 35 boys, all between 1 and 18 years of age. Sixteen of the group had pituitary myxedema; the rest had varying degrees of primary hypothyroidism. Most of the children in this group showed pronounced physical signs of thyroid deficiency, together with abnormally low basal metabolic rates and I^{131}-uptake and protein-bound iodine values. Their bone ages ranged between one and four years below their chronological ages. Moreover, some of these children also had serious nonthyroid disorders, such as mental retardation, mongolism, and cerebral palsy.

Prior to this investigation, all of the 100 patients had been treated with thyroid extract and thyroglobulin (average dose: 3 grains [192 mg.] daily) and with thyroxin (average dose: 0.2 mg. daily). Ten of the children had been treated with these preparations for as long as two years with only incomplete remission of symptoms. Also, the previous preparations had caused reactions such as palpitations, headache, and changes in behavior in 22 of the 100 children. In all patients, at least one month had elapsed between withdrawal of all previous drugs and administration of liothyronine. Thus, the possibility of carry-over effects from previous treatments was eliminated.

Initial dosage of the drug was 5 mcg. daily during the first week of the study. If the patient's tolerance permitted it, the dosage was increased to 10 mcg. daily the second week of therapy and then to 15 mcg. daily during the third week. The fourth week was then set aside as a rest period, and no medicament was given. For the second month of treatment, 25 mcg. of liothyronine daily was given as the initial dose for the first week. If the patient could tolerate an increase, 50 mcg. daily was given for the next two weeks. The tolerated maintenance dose of 50 mcg. or less was then continued for three weeks of the third month. At the end of the third month, the results were evaluated.

Results of Treatment

Responses to treatment with liothyronine were evaluated by the following criteria. They were considered to be excellent when all or 90% of the patient's symptoms subsided during treatment; to be good when 70 to 90% of the symptoms subsided; to be fair when at least 50% of the symptoms subsided; and to be poor when less than 50% of the patient's symptoms subsided

during treatment. These ratings were based on improvements in behavior, circulation, muscle and joint function, skin texture, appetite, bowel function, and bone maturation, when it was measurable.

Metabolic Insufficiency.—The results of the treatment in the 40 patients with metabolic insufficiency were excellent in 22, good in 15, and fair in 3. During treatment, the attitude and behavior of the children in this group generally became normal. Every patient improved in appetite and bowel function and gained about 2½ lb. (1,134 gm.). During the three months of treatment, the bone age of most of these children increased about six to nine months; these increases were about 100 to 200% more than the growth expected in normal children of the same ages. Cholesterol levels generally decreased, and basal metabolic rates increased to normal levels. The over-all clinical responses were most encouraging and dramatic, as illustrated by the following case history.

CASE 1.—A 7-year-old boy was brought for examination primarily because his parents had difficulty getting him to eat. On casual observation, he appeared to be essentially normal, although he was slightly underweight and short for his age. On closer examination, his hair was seen to be slightly dry, and his skin was rough. His hands were unusually cool. His elbows and knees were hyperkeratotic, and there was some spotted eczema. The patient's parents reported that he was frequently constipated, tired, and unduly inactive. He seemed to show little interest in normal activities and did poorly in school.

His bone age was approximately four years, indicating a retardation of 36 months. The protein-bound iodine level was normal—7.6 mcg. per 100 cc. of serum. The serum cholesterol was high normal, 230 mg. per 100 cc., and other laboratory tests were normal. The basal metabolic rate ranged between —12 and —15% on repeated tests.

Prior to this study, the patient was treated with 3 grains of desiccated thyroid daily and subsequently with 0.2 mg. of thyroxin daily over a period of 12 months. During this time, there was some slight improvement in the patient's clinical picture, but the over-all response was considered inadequate. Previous medication was stopped for six weeks, then liothyronine was given in doses that were gradually increased up to 50 mcg. daily. During the next three months, the patient's appetite increased, and he became less constipated and gained 6 lb. (2.7 kg.). There was a reduction in hyperkeratosis of the skin, and his hair became smoother. The boy's parents stated that he seemed to show more interest in activities, his grades at school improved, and he was sleeping better. He was more alert and attentive and seemed more cheerful. His bone age increased approximately six months, indicating a maturation rate of about twice that expected in normal children. The patient's condition has remained improved.

Hypothyroid Disorders.—The 60 children with hypothyroidism and related disorders showed the following responses to liothyronine: excellent in 35, good in 22, fair in 2, and poor in 1. To illustrate excellent and good responses to liothyronine, several typical case histories are presented.

CASE 2.—A mentally retarded 6-year-old boy with organic brain disease showed evidence of severe hypothyroidism. His bone development was delayed by two years, and he had hyperkeratosis, wedge-shaped teeth, constipation, and disorientation. After three months of treatment with liothyronine, he was placid, he had an increased attention span, and his bowel function and skin texture were normal. He had grown 1½ in. (4 cm.) (three times the growth of a normal child of the same age during a three-month period), and he had gained 3 lb. (1.3 kg.).

CASE 3.—A dwarfed 6-year-old boy was originally given a diagnosis of diabetes insipidus at the age of 3. During the following three years, he had received 5 cc. of vasopressin (Pitressin) tannate per week. At the age of 6, his height was equal to that of a 4½-year-old boy, and his bone maturation was equal to that of a 2-year-old child. Other symptoms included dry hair and skin, frequent asthmatic episodes, polyuria, and polydipsia. His urinary output per day, without treatment, averaged 5,000 to 6,000 cc., with a specific gravity of 1.001 to 1.002. He was started on therapy with 5 mcg. of liothyronine daily, which was later increased by increments of 5 mcg. daily up to 15 mcg. After three weeks, his urinary output decreased to 1,500 to 2,000 cc. per day, and the specific gravity of the urine increased to 1.026 to 1.030. He required only 1 cc. of vasopressin tannate per week. His symptoms of fatigue disappeared; his appetite and bowel function became normal; his symptoms of asthma and dry hair and dry skin subsided. He grew 1 in. (3 cm.) in three months (an increase on the Burgess chart from 5% up to 10%), and two new ossification centers appeared in the carpal bones. Thus, his bone age increased nine months during the three months of treatment. When the dosage of liothyronine was increased to 25 mcg. daily, his urinary output increased to 4,000 cc. per day, the specific gravity of the urine decreased to 1.002, and he required 4 cc. of vasopressin tannate per week. However, when the dosage of liothyronine was cut to 15 mcg. daily, improvements were again obtained.

CASE 4.—An achondroplastic 2-year-old boy presented the typical symptoms of hypothyroidism: dryness of the hair and skin, constipation, and poor appetite. He had no ossification centers for skeletal maturation. On a maximum dose of 25 mcg. of liothyronine daily, he gained 2 lb. (907 gm.) and grew 1 in. in three months (twice the expected growth of a normal child during this time). The first two carpal centers of ossification and second molars appeared; his skin and hair became normal, his appetite improved, and his bowel function became normal.

CASE 5.—A 9-year-old mongoloid girl was underdeveloped and had a bone age of a 5-year-old. With a maximum dose of 50 mcg. of liothyronine daily, she became alert, her hair and skin became normal, and her macroglossia receded. Also, she improved in emotional behavior, speech, and ability to concentrate. Her increase in height was 2% on the Burgess chart, and her growth in bone age was about six months (100% more than the expected bone age increase of a normal child of the same age).

CASE 6.—A 7-year-old boy had severe symptoms of cerebral palsy: hemiplegia, rigidity, ataxia, athetosis, and retardation in speech. He had a delayed ossification development of two and a half years below normal. With a maximum dose of 25 mcg. of liothyronine daily he became calm and relaxed, so that rehabilitative measures could be performed at the end of the third month. Concurrently, his bone age increased by six months (100% more than expected in a normal child of the same age.)

Comment

The clinical efficacy of liothyronine in this study was impressive in treating both the patients with metabolic insufficiency and those with hypothyroidism. Almost universally, liothyronine gave striking improvements in behavior, circulation, appetite, hair and skin texture, and bowel function. Furthermore, in many patients, liothyronine stimulated bone growth as much as 200% beyond that expected for normal children of the same ages. All of these 100 children had been treated previously with the standard thyroid preparations during a comparable three-month period. By comparing responses to the various therapies, it was found that, in clinical use, 50 mcg. of liothyronine daily is roughly equivalent to 200 mcg. of L-thyroxin daily and to 3 grains of thyroid extract or thyroglobulin daily. This comparison is in agreement with that reported by Frawley and his co-workers,[9] who used liothyronine in the treatment of myxedema in adults; 75 to 100 mcg. of liothyronine daily was reported to exert a calorigenic effect equivalent to that of 200 to 300 mcg. of

L-thyroxin daily and of 96 to 192 mg. (1½ to 3 grains) of thyroid extract daily. It appears, however, that therapeutic doses of liothyronine for children are about one-half to one-fourth of that required for adults.

In general, clinical response appeared to occur more rapidly with liothyronine than with previous therapies. This rapid response, reported also by other investigators,[10] implies that liothyronine may be used as a diagnostic aid. If a patient believed to have hypothyroidism or metabolic insufficiency is given liothyronine, clinical improvement should occur within two to three weeks. There has been widespread speculation by many investigators[11] that liothyronine is the ultimately active thyroid hormone. This theory seems to be supported by the results of the present study, because liothyronine gave more rapid therapeutic responses than previous preparations had given and it was effective in treating many children whose conditions were resistant to other preparations.

None of the 100 children in this study developed side-reactions to liothyronine, whereas 22 had done so after treatment with previous therapies. Since the same regimen of therapy was used in this study, it is concluded that therapeutic doses of liothyronine cause fewer side-reactions than therapeutic doses of thyroid extract, thyroglobulin, and thyroxin. The method of administration probably reduced side-reactions to liothyronine as well as to the other thyroid preparations given previously. A very small dosage (5 mcg. daily) of liothyronine was given at the start of treatment; afterwards, the dosage was gradually increased in small increments until the therapeutic level was reached. Secondly, the cyclic method of administration, with a rest period during each month, was used. Adopted on the basis of extensive calorigenic studies with desiccated thyroid by Handelsman and Gordon in 1939-1940,[12] this method allows for proper control of the individual's response while the therapeutic dosage level is being reached. My experience has been that exacerbation of symptoms never occurs during the rest period of each month and that an individual's tolerance to metabolic stimulants can be increased in this way.

Summary and Conclusions

A study was conducted on 100 children to determine the clinical effects of a new thyroid-like hormone, sodium liothyronine (L-triiodothyronine), in treating metabolic and hypothyroid disorders. The patients in this study ranged from 1 to 18 years of age. Forty of the patients were given a diagnosis of metabolic insufficiency; the other 60 of hypothyroidism. All children in both groups had been treated previously with thyroid extract, thyroglobulin, and thyroxin. The average dose of liothyronine varied from an initial dose of 5 mcg. daily to a maximum of 50 mcg. daily, with a mean dose of 15 to 25 mcg. given daily for three weeks of each month in this three-month trial. The 40 patients with metabolic insufficiency showed the following responses to liothyronine: 22, excellent; 15, good; 3, fair. The 60 patients with hypothyroidism showed the following responses: 35, excellent; 22, good; 2, fair; and 1, poor. In both groups of children, liothyronine brought about rapid clinical improvement, particularly in those children whose conditions were refractory to standard thyroid preparations.

From all results of this preliminary study, it is concluded that administration of liothyronine is an effective, safe, and well-tolerated form of treatment for metabolic insufficiency and hypothyroidism in children. Further studies of this compound seem warranted and are recommended.

Addendum

Since the foregoing report was prepared, the patients here described have been treated with liothyronine for an additional nine months. During this time, the relief of signs and symptoms of metabolic insufficiency and hypothyroidism, the acceleration of bone development, and the emotional and mental benefits of liothyronine have been sustained. In 10 patients, the dosage of liothyronine was increased to 75 to 100 mcg. daily in an attempt to obtain optimum response. When this was done, side-effects such as hyperirritability, headache, insomnia, and palpitations occurred in five of these patients. These reactions disappeared with subsequent reduction in dosage. The degree of response remained essentially unchanged in the other five patients. The condition of none of the children in the group has become refractory to treatment. Additional details of the extended study are to be reported in the future.

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TREATMENT OF TEMPORAL ARTERITIS WITH ADRENAL CORTICOSTEROIDS

RESULTS IN FIFTY-FIVE CASES IN WHICH LESION WAS PROVED AT BIOPSY

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• *Temporal arteritis, with the exception of ocular manifestations, is a self-limited and benign condition; therefore, treatment and prevention of the associated visual loss should be the immediate and primary consideration. It is believed that cortisone and the related steroids will control temporal arteritis as long as it endures, and will at least prevent progression of any loss of vision that may exist at the time of diagnosis. The optimal dose and duration of treatment with adrenal corticosteroids have not, as yet, been adequately defined. Relapse may occur in some instances when the daily dose of cortisone is lowered beyond a certain point, usually 100 mg.*

During the past six years, a number of patients with temporal arteritis that was proved by biopsy have been treated with adrenal corticosteroids at the Mayo Clinic. Most patients received cortisone, either parenterally or orally, but a few patients seen more recently received prednisone. It has seemed worthwhile to report the effects of this type of treatment on the systemic manifestations of temporal arteritis and particularly on the ocular lesions.

General Considerations

The syndrome known as "temporal arteritis" was first delineated as a clinical entity by Horton, Magath, and Brown [1] in 1932, although two instances of the condition were observed prior to that time.[2] Since these earliest reports, more than 250 cases have been recorded in the literature, and the disease is now included in some of the standard medical textbooks. Recent medical literature has included a number of excellent reviews of the subject.[3]

Despite intensive study, the causation of the disease remains unknown, and little has been added to the first description of temporal arteritis except in three aspects. First, it has become apparent that the arteritis may not be confined to the temporal or even to the cranial arteries. Lesions identical to those seen in the temporal arteries have been found in the aorta, carotid and pulmonary arteries, and in other peripheral and visceral arteries.[4]

Second, it has been recognized that temporal arteritis is not an entirely benign condition, for there have been reports of deaths occurring during the course of the disease.[3c] Not all of the deaths, however, were caused by the arteritis itself. Because the disease affects the elderly, and because it frequently is difficult if not impossible to determine the exact cause of death, there is no general agreement as to the true mortality rate of the disease. There is widespread agreement, however, concerning the frequency and seriousness of the most common and most severe feature of temporal arteritis, aside from the involvement of the temporal arteries themselves; namely, involvement of the visual apparatus, leading in all too many cases to permanent blindness.[5]

Third, some progress has been made in the methods of treatment of this disease. It was recognized, in the early days of the treatment of temporal arteritis, that sectioning of the involved artery for biopsy frequently produced relief of the head pain. On the basis of this observation, injection of procaine hydrochloride along the course of the involved temporal artery has been tried, and striking relief of pain has been reported to follow it.[6] Benefit also has been reported from the intravenous administration of histamine [7] and from the use of chlortetracycline.[8] For the most part, however, treatment remained mainly supportive and nonspecific. With the advent of the adrenal corticosteroids, a new approach to the treatment of temporal arteritis was possible. Since the first trial of cortisone against this disease,[9] evidence has been accumulating that cortisone and related steroids exert a favorable effect upon the signs and symptoms of temporal arteritis, and it appears that at present the use of these hormones is the treatment of choice.[10]

Temporal arteritis remains a problem to the clinician for several reasons. The disease may be difficult if not impossible to recognize in its early stages, before obvious involvement of superficial arteries occurs. The number of reported cases in which patients were adequately treated with adrenal corticosteroids is relatively small, so that the effect of such treatment, particularly in regard to the visual complications, is not

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clear. Finally, the optimal dose and duration of treatment with adrenal corticosteroids have not been adequately defined.

Present Study

In the present series of 55 patients, the clinical diagnosis of temporal arteritis was confirmed in every case by microscopic examination of a section of tissue from one of the superficial cranial arteries. There were 28 men and 27 women. The oldest patient was 83 years old and the youngest was 60 years old. All sections for biopsy were taken with the use of local anesthesia. Whenever possible, the biopsy specimen was taken from a site where the artery appeared abnormal or was abnormal to palpation. In some instances, the first frozen section studied at the time of biopsy indicated either that the artery was normal or that the results were inconclusive. In such cases, study of another section taken farther along the course of the artery disclosed the typical pathological picture of temporal arteritis, demonstrating the frequently spotty arterial involvement in this disease. For this reason, repeated biopsy specimens always should be obtained when the presence of the disease is strongly suspected and results of the first biopsy are negative.

Cortisone therapy was begun as soon as the diagnosis was suspected. Previous experience has shown that it is neither necessary nor advisable to withhold cortisone therapy until biopsy has been done.[10a] Usually, 300 mg. of cortisone was given intramuscularly on the first day of treatment, followed by 150 to 200 mg. injected intramuscularly daily thereafter, either in one injection or in divided doses every 12 hours. In some cases, treatment was continued by the intramuscular route, but in the majority of instances the mode of administration was changed to the oral route after subsidence of symptoms and decrease of the erythrocyte sedimentation rate to normal or nearly normal. When the oral route was used, the same total daily dose of cortisone was administered, but it was given in fractions every four to six hours. Whenever possible, cortisone therapy was continued, with daily doses of 150 to 200 mg. for six weeks. At the end of this period, the daily dose of cortisone was altered by decrements of 12.5 to 25 mg. every three to four days, provided the clinical progress of the patient was satisfactory and the erythrocyte sedimentation rate remained within normal or nearly normal limits. When the total daily dose was reduced to 12.5 mg., administration of the drug was discontinued. A few patients were treated entirely with orally administered cortisone in the same dosage as previously described. Three patients were treated with prednisone, the dosage beginning with 75 mg. the first day and then continuing with 50 mg. daily in divided doses every four to six hours for six weeks. At the end of this time, the total daily dose was altered by decrements of 2.5 mg. every three or four days until administration of the drug could be discontinued.

In several patients, relapse occurred when the daily dose of cortisone was lowered beyond a certain point, usually around 100 mg. In these cases it was necessary to increase the dose of the hormone for from several days to a week or more and then to attempt again to reduce the amount gradually, as described above. In one case, three separate attempts were made to decrease the daily dose of cortisone to less than 75 mg. before success was achieved. Treatment in this case required a total of 15 months. Several other patients required treatment for 9 to 12 months before administration of the drug could be discontinued.

All patients who received cortisone were maintained on a 2-gm. sodium diet to minimize retention of fluids, and most patients were given from 3 to 6 gm. of potassium chloride daily to prevent hypokalemia.

There were no serious complications from such long-term intensive cortisone therapy. Only once was it necessary to stop the use of the drug completely, in a 66-year-old woman who had previously received subshock insulin therapy for a depressive psychotic reaction. After five days of cortisone therapy she became euphoric and disoriented, and administration of the drug was discontinued. One other patient exhibited mild euphoria, mild "Cushing-syndrome-like" features developed in two patients, and one patient had transient memory and speech difficulty while receiving cortisone. In one patient, who had diabetes mellitus, the requirement of insulin was increased during the period of therapy. Intermittent, mild edema of the ankles developed in only six patients.

The perplexing combination of vague, nonspecific symptoms and the pathognomonic findings in the temporal arteries has been well documented previously by others. It seems pertinent, however, to reemphasize the diverse ways in which the physician may be challenged by this entity. The following brief case reports are presented to demonstrate this aspect of the problem.

Report of Cases

Case 1.—A 64-year-old woman was admitted to the clinic with a three-month history of weakness, fatigue, malaise, and a temperature as high as 104 F (40 C). Five weeks before her admission she had noted painful, tender, red nodules in both temporal regions associated with a moderately severe bilateral temporal headache. She had received large doses of several antibiotic agents and sulfonamides without benefit. When she was admitted, her temperature was 100 F (37.8 C). Both temporal arteries were noted to be pulsating. The right temporal artery was indurated but not hypersensitive to palpation, nor was the overlying skin inflamed. Funduscopic examination revealed a cotton-wool patch in each retina. The erythrocyte sedimentation rate was 132 mm. in one hour (Westergren). A biopsy specimen from the right temporal artery showed temporal arteritis.

This typical instance of temporal arteritis illustrates the systemic symptoms and the degree of fever that may be associated with this disease. It should be noted that this patient had had generalized symptoms for approximately seven weeks prior to the appearance of the diagnostic signs of redness, hypersensitivity to palpation, and induration overlying the temporal arteries. The diagnostic possibilities that might have been considered before the appearance of these signs are apparent, as is the lack of response to a number of antibiotic agents and sulfonamides.

The cotton-wool patches in the retinas of this patient may have been of the so-called toxic variety seen in the presence of some of the collagen diseases. But it is more probable that they were manifestations of mild ischemia of the retina caused by arteritic involvement

of the ophthalmic or central retinal arteries. In a patient who presented similar lesions on admission to the clinic but who was not treated with cortisone, complete bilateral blindness developed as the result of progressively increasing ischemia of the optic nerves. In the case just described, the cotton-wool patches resolved and no further evidences of ischemia developed.

CASE 2.—A 74-year-old woman had been well until a month before admission to the clinic; then she began to experience aching in the muscles of both legs, thighs, shoulders, and arms. One week later pain in the jaw, malaise, night sweating, and headache developed, and her temperature increased to 102 F (38.9 C). During the same time, the patient experienced an episode of double vision that lasted for five days. On admission, the patient appeared to be in moderate distress. Her temperature was 100 F. The scalp overlying the occipital arteries was hypersensitive to touch, red, and indurated. Pulsations in the occipital arteries were present but were diminished. The erythrocyte sedimentation rate was 122 mm. in one hour (Westergren). A biopsy specimen from the right occipital artery disclosed arteritis consistent with temporal arteritis.

Systemic symptoms predominated in the foregoing case also, with widespread aching in muscles, including the muscles of mastication, being the most prominent feature. Muscle aching preceded the pain in the head. This patient also described somewhat atypical attacks of transient loss of vision of short duration. Examination of the ocular fundi showed nothing of significance. Since the diplopia of this patient was of such short duration, it may simply have been the result of a nonspecific exaggeration by illness of a previously present ocular muscle imbalance. However, as will be noted later, two of the patients in this series did have definite, acquired weakness of extraocular rotations, probably as a manifestation of temporary ischemia of the muscles.

CASE 3.—A 71-year-old man had been in good health until six weeks before his admission, when a moderately severe infection of the upper part of the respiratory tract developed, associated with malaise, sore throat, cough, bitemporal throbbing headache, and a temperature of 100 F. During the next two weeks the respiratory infection subsided, but malaise, cough, headache, and fever persisted. At the same time, the patient had noted prominent, tender, red nodules in both temporal regions. He had received penicillin and chloramphenicol, without benefit. When admitted, this patient was in moderate distress. His temperature was 99 F (37.2 C). Both temporal arteries were prominent, and the skin overlying them was red, hypersensitive to touch, and indurated. Pulsations in both arteries were diminished. The erythrocyte sedimentation rate was 118 mm. in one hour (Westergren). Biopsy of tissue from the right temporal artery showed temporal arteritis.

In this patient, temporal arteritis began with moderately severe infection of the upper part of the respiratory tract. This mode of onset has been noted by other authors. The interval between the respiratory infection and the onset of the more characteristic symptoms and signs of temporal arteritis may be longer than it was in this case. On the basis of such cases some authors have suggested that infection may be an inciting if not an etiological factor in the disease. This patient experienced no ocular disturbances other than a period of diplopia that lasted only a few hours, about two weeks before his admission to the clinic. Objectively, vision was normal. Ophthalmoscopic examination revealed only mild narrowing and sclerosis of the retinal arterioles.

CASE 4.—A 69-year-old man had stumbled and struck his forehead against a wooden case. He had not become unconscious, and immediately afterward he had felt well. Three days later, occipital headache developed and soreness arose in the posterior aspect of the neck. These had been followed by soreness in the muscles of the jaws, lasting several days. About six weeks after the patient had struck his head, diplopia developed that lasted three days and then disappeared. A week after this, the results of a complete physical examination, including extensive neurological studies, were within normal limits. The patient obtained relief from the aching by the use of heat and massage to the neck. However, two and a half months after the injury to the head, severe, constant frontal headache developed. During the next seven days there were four episodes of sudden and complete loss of vision in the left eye. Each episode lasted about 10 minutes, and the return of vision was complete after each. The patient believed his headache was more severe during the transient episodes of blindness of the left eye. Because of this development he returned to the clinic for reexamination. Temperature was normal. A pulse was not palpable in either temporal artery. There was no induration or redness, and the patient did not recall any unusual prominence in the vicinity of either temple. Vision was 6/6 and 14/21 in each eye, and the fields of vision were normal. The ocular fundi were normal. The erythrocyte sedimentation rate was 104 mm. in one hour (Westergren). A biopsy specimen from tht left temporal artery showed temporal arteritis.

The history in this case was complicated by the injury to the head. The diplopia and headache might easily have been attributed to this trauma. However, the episodes of transient amaurosis were not so easily explained, and further investigation produced the correct diagnosis. As far as can be learned, acute involvement of the temporal arteries of this patient never was conspicuous. The attacks of transient amaurosis in this patient were more nearly typical than were those in the patient in case 2; evidently they were caused by transient insufficiency of the blood supply to the left retina. The attacks ceased while the patient was under treatment at the clinic. Such episodes of transient loss of vision have been noted to occur in association with partially occlusive lesions of the internal carotid artery.[11]

CASE 5.—A 73-year-old man said he had had weakness, malaise, anorexia, and intermittent, severe frontal and occipital headaches for five weeks before his admission to the clinic. Thirteen days before his admission he had noted diplopia, and three days after this all vision in the left eye suddenly had been lost. At admission, the patient had a normal temperature, but prominence and tenderness of both temporal arteries was noted. Pulsations could not be felt in either temporal artery, but neither redness nor induration was present. Vision of the right eye was 6/15 and 14/21, and the field of vision was severely constricted; the left eye was blind. The optic disks were edematous; they were elevated to 1 D. and were rather pale. The retinal arterioles were slightly narrowed and sclerosed. The erythrocyte sedimentation rate was 92 mm. in one hour (Westergren). A biopsy specimen from the left temporal artery disclosed temporal arteritis.

The history in this case is characteristic of all too many cases of temporal arteritis in which the diagnosis is not suspected until after blindness has occurred in one eye or both eyes. The ischemic type of optic neuritis present in this case is the most typical ocular lesion seen in association with temporal arteritis. The patient obtained almost complete relief from the general symptoms soon after the institution of cortisone therapy, and the vision of the right eye was somewhat improved subjectively. Reexamination of the eyes four months after the patient's first admission showed that

the vision of the right eye was 6/10 and 14/21 and that the field of vision had widened considerably. The left eye was still blind. The optic disks were pale but were no longer edematous.

CASE 6.—An 80-year-old man had been well until three weeks before his admission to the clinic. At that time, a cold developed that lasted several days. During the time he had coryza, he had received one injection of penicillin, without much benefit. Seven days before his admission he lost the vision of the right eye within a period of several hours. Two days later he suddenly lost the vision of the left eye. He said he had not had pain in the head, and did not recall any tenderness or nodularity of the temporal arteries.

We found the patient to be completely blind. Temperature was normal. Both temporal arteries were patent and normal to palpation. Ophthalmoscopic examination revealed both optic disks to be edematous, with blurred margins. All retinal vessels appeared essentially normal. There were two small hemorrhages in the peripheral area of the right retina and one in the left. Biopsy of tissue from the right temporal artery revealed temporal arteritis. Cortisone therapy was instituted soon after the patient was admitted, but vision did not return. Such has been our experience in all cases in which the eye was totally blind before treatment was started.

The prevention of such a tragedy as occurred in this case seems almost impossible in view of the present state of our knowledge. Furthermore, the normal appearance of the temporal arteries would give even the most astute physician an ill-starred sense of security in excluding this disease, had it entered his differential diagnosis.

TABLE 1.—*Ocular Involvement in Fifty-five Cases of Temporal Arteritis*

Ocular Involvement	Patients, No.
Due to temporal arteritis	
Ischemic optic neuritis	18
Retrobulbar neuritis	1
Optic atrophy	2
Toxic retinopathy	2
Ocular-muscle paresis	2
Transient amaurosis without permanent visual loss	7
Total	32
Not due to temporal arteritis	
Occlusion of retinal tributary venule	2
Macular degeneration	1
Total	3

Effects of Treatment on Systemic Manifestations

There were no fatalities among this series of 55 patients. In all cases in which generalized symptoms such as weakness, malaise, and fatigue were present at the beginning of therapy with adrenal corticosteroids, these symptoms gradually abated during the first few days. Seven patients had an elevated temperature when first admitted to the clinic and at the time treatment was started. The temperature of five of these patients became normal within 24 hours after the institution of hormone therapy; the temperature of one patient remained elevated for 3 days, and another patient had a low-grade fever for the first 10 days of treatment. Nine patients complained of aching of the muscles of the extremities, neck, and shoulders prior to treatment. All but two were relieved within a few days. Of these two, one continued to have generalized aching for six days after treatment was started, and the other complained of intermittent muscular aching throughout the period of treatment. Twenty-one patients had pain in the head with or without tenderness of the scalp when treatment was begun. The headache of 18 patients was ameliorated within the first 48 hours. Two patients said that most of their headache was relieved by the taking of biopsy specimens, but the other patient continued to complain of headache during the remainder of treatment.

Thus, exclusive of ocular complications, most patients with temporal arteritis can be expected to become relatively asymptomatic within a few days after treatment is started with cortisone or related adrenal corticosteroids in adequate doses. However, our observations in the present series of cases would seem to confirm the previous opinion that the adrenal corticosteroids merely suppress the manifestations of temporal arteritis but do not actually alter the course of the disease.[10a] This was borne out in several instances in which symptoms recurred after a varying period of treatment as the dose of the hormones was reduced below a critical value. Furthermore, results of follow-up biopsy in several of our cases revealed characteristics of subacute or chronic arteritis that evidenced little more healing than would be expected in the natural course of this disease.

Effects of Treatment on Ocular Lesions

Thirty-five of the 55 patients had some type of ocular involvement, as indicated in the history or disclosed by examination. These lesions are listed in table 1. The occlusions of tributary retinal veins that were present in two patients and the bilateral macular degeneration noted in one patient probably were not related definitely to the temporal arteritis. In the remaining 32 patients (58.2% of the total group), the ocular involvements seemed to be definitely parts of the syndrome of temporal arteritis. In 21 of these (or 38.2% of the group of 55), there was loss of vision of varying degree. The most common cause of the loss of vision was ischemic optic neuritis, which was present in 18 patients. The optic neuritis was of the retrobulbar type in one patient. Optic atrophy secondary to optic or retrobulbar optic neuritis was noted at the time of the first examination in two patients. In 20 of the 21 patients, objective loss of vision was present at the time of admission; in one patient the onset of visual loss occurred seven days after treatment with cortisone was begun. One other patient who could see only movements of the fingers with his left eye on admission lost the remaining vision in this eye after 10 days of treatment with cortisone.

The data concerning visual loss in the present series are summarized in table 2, in which there are also presented for comparison the findings in a similar group of 53 patients with temporal arteritis seen at the Mayo Clinic prior to the introduction of cortisone and related steroids and data concerning a group of 250 patients reported upon in the literature. A few of this last group also were treated with cortisone. In the present series, five patients were blind in both eyes and six were blind in one eye when first seen at the clinic. Vision was not regained in any of these 16 eyes. Reduction of vision of varying degree, but not to the

point of blindness, was present in 16 eyes at the time of admission of the patients. Under treatment with cortisone the vision was improved in seven, remained unchanged in five, and deteriorated somewhat in four.

In the group of patients treated with adrenal corticosteroids, the number of those bilaterally blind at the time of dismissal was no greater than the number of those bilaterally blind at the time of admission, and there were only two additional blind eyes, an increase of 12.5% in respect to blind eyes. In contrast, in the group seen prior to the introduction of steroid therapy there was a threefold increase in the number of patients with bilateral blindness during the period of treatment and a 50% increase in the number of blind eyes, from 16 to 24, in the course of treatment. Among patients seen before hormone therapy became available, five who were blind in one eye at the time of admission became blind in the remaining eye while under observation. There were no similar occurrences among those patients receiving hormone therapy. On the basis of the findings in 250 cases reported in the literature, it might be expected that bilateral blindness would develop in 22% of cases of temporal arteritis. It occurred in 17% of the Mayo Clinic patients not treated with cortisone and in only 9% of those treated with adrenal corticosteroids.

TABLE 2.—*Visual Loss in Present Series of Fifty-five Patients Compared with Loss in Fifty-three Patients Seen Prior to Cortisone Therapy and Loss in 250 Cases from Literature**

Condition	Cortisone Used (55 Patients), Condition at		Before Cortisone (53 Patients), Condition at		Literature (250 Patients), Condition at	
	Admission	Discharge	Admission	Discharge	Admission	Discharge
Normal vision	35	34	33	30	144	129
Bilateral blindness	5	5	3	9	42	54
Unilateral blindness	6	8	10	6	19	13
Blind eyes, no.	16	18	16	24	103	121
Bilateral loss of vision without blindness	3	2	6	7	23	38
Unilateral loss of vision without blindness	6	6	1	1	22	16
Patients with blindness and lesser visual loss, total no.	20	21	20	23	106	121
Patients with blindness and lesser visual loss, %	36.4	38.2	37.7	43.4	42.4	48.4

* References to the articles from which these 250 cases were collected will be furnished on request.

Comment

Our primary purpose in undertaking this study was to ascertain the value of cortisone and related adrenal corticosteroids in the prevention and treatment of the ocular manifestations of temporal arteritis. Since we believe that, in respects other than ocular, temporal arteritis is primarily a self-limited and benign condition, prevention and treatment of the associated visual loss are of paramount importance. All but a very few patients in this series were promptly relieved of their other symptoms by the administration of cortisone or prednisone.

All 55 patients in the current series were examined funduscopically at least once, and those who had visual symptoms received many such examinations. Visible edema of the optic disks was present in 18 of the 21 patients who had loss of vision, and pallor of the disks was present in the other 3. Loss of vision in all cases probably was due to extreme narrowing of the lumens of the ophthalmic or central retinal arteries. This does not necessarily mean that thrombosis or complete occlusion of the vessels had occurred, but it does mean that narrowing was sufficient to cause anoxic damage to the optic-nerve fibers.

Among the 21 patients who had sustained permanent loss of vision, there were some in whom transient obscurations of vision of short duration had occurred in one eye or both eyes prior to the onset of the persistent loss. Similar episodes of transient amaurosis had occurred in seven additional patients before treatment was started (table 2); permanent loss of vision did not develop in any of these patients. Such episodes may result from arterial spasm or transient circulatory insufficiency in the retina secondary to lesions in the internal carotid as well as in the ophthalmic or central retinal arteries.

The so-called toxic cotton-wool patches seen in two of the patients in this series (table 1) probably result similarly from insufficient blood supply to the retina, since they were present also in the second eye of one of the patients who had unilateral loss of vision associated with ischemic edema of the optic disk.

Involvement of the blood supply to the extraocular muscles also seems to be a part of the syndrome of temporal arteritis, for several of the patients complained of more-or-less transient episodes of diplopia, and definite, objective disturbances of ocular rotation were noted in two cases. It seems probable that ischemia of the extraocular muscles may result from arteritic involvement, either of the ophthalmic artery itself or of its branches to individual muscles. The diplopia cleared rapidly under treatment in each instance.

Occlusion of a small tributary venule was noted in one retina of each of two patients (table 1). It seems probable that these occlusions were secondary to retinal arteriolosclerosis rather than to arteritis. One patient had relatively poor vision as a result of a senile type of macular degeneration (table 1), obviously unrelated to the temporal arteritis.

As previously stated, 20 patients of the present series had sustained visual loss before they were admitted to the clinic. The final incidence of bilateral blindness in the present group was 9%; it was 17% in a previous group of patients seen at the clinic prior to the use of cortisone; and it was 22% in a group of 250 cases collected from the literature. A comparison of these figures would seem to indicate that the administration of adrenal corticosteroids in the early

phases of the disease may reduce the incidence of serious ocular involvement. Speculation immediately arises, therefore, if it is possible to determine beforehand, on the basis of the early signs and symptoms, which patients with temporal arteritis eventually will suffer visual impairment. Such a determination seems impossible when the following aspects of the sequence of events in this disease are reviewed.

In general, ocular symptoms began within three to six weeks after the beginning of headache and a somewhat shorter interval after the appearance of induration and hypersensitivity of the temporal arteries. However, some patients in this series had both headache and prominent, indurated, hypersensitive temporal arteries and at no time had any ocular symptoms. In some instances, visual loss occurred within a month of the appearance of such vague generalized symptoms as fever, malaise, and aching of muscles.

In the present study, we were unable to establish any credible correlation between the presence or absence of a pulse in the involved temporal artery and visual loss on the same side when the visual loss was unilateral. The occurrence of blindness did not correlate well with the severity of temporal-artery involvement. There was some tendency for the loss of vision to occur on the side of the more severely involved temporal artery when both arteries were involved. The more severely involved temporal arteries tended to be more painful. Visual loss also occurred in both eyes when headache was unilateral. Finally, a number of patients had diplopia or transient amaurosis, even in repeated incidents, without the development of any permanent visual loss.

It is apparent, then, that it is unwise to attempt to select only certain patients with temporal arteritis for hormonal treatment. The present policy at the Mayo Clinic is to begin to treat immediately all patients suspected of having temporal arteritis with either cortisone or one of the related adrenal corticosteroids. In fact, treatment is begun prior to biopsy, if the latter procedure involves any delay. We prefer the intramuscular route of administration of cortisone for the first week or so of treatment because of the sustained high levels that it produces. If results of adequate biopsy prove negative, treatment can be interrupted with no harm having been done. At the present state of our knowledge of temporal arteritis, the foregoing seems to be the soundest approach to the problem.

In the past, we have not routinely administered anticoagulant agents to patients with temporal arteritis. We feel, however, that the combined use of anticoagulants and adrenal corticosteroids might be indicated and might be of value in certain instances, notably for patients who have sustained recent impairment or loss of vision in one eye. It is conceivable that in such cases inflammatory changes already may have developed in the ophthalmic artery of the presumably uninvolved eye and that subsequent thrombosis with loss of vision might supervene, with or without steroid therapy. The intermittent inhalation of 100% oxygen has seemed to be of some benefit in patients with acute or recent visual impairment, but we have not been impressed with the value of vasodilating drugs or stellate-ganglion blocks in such cases.

Summary and Conclusions

Fifty-two patients with temporal arteritis proved by biopsy were treated with cortisone and three other patients with this syndrome were treated with prednisone. There were no deaths. The local and systemic symptoms of most of these patients were promptly relieved. Thirty-one (56%) of the 55 patients, at the time of admission to the clinic, had ocular involvement that was considered to be a part of the syndrome of temporal arteritis. Twenty patients (36.4% of the whole group) had some loss of vision at the time of admission. In this group of 20 patients, 5 had bilateral blindness and 6 had unilateral blindness. The condition of none of the blind eyes improved under treatment. However, bilateral blindness did not develop in any patient during treatment. The percentage of the occurrence of bilateral blindness increased from 6 on admission to 17 at the time of discharge in the previous group of patients with temporal arteritis seen at the Mayo Clinic prior to the advent of adrenal corticosteroid therapy, and this percentage increased from 17 to 22 in a group of cases collected from the literature.

We believe that the use of cortisone or a similar adrenal corticosteroid is definitely indicated at present in the treatment of temporal arteritis and that the agent should be administered to all patients who have this disease. We are in accord with the conclusions of Whitfield and associates[10c] that the chief value of cortisone and related steroids in the treatment of temporal arteritis is to control the arteritis as long as it endures and thus to safeguard the degree of vision that remains. That these hormones promote histological healing, however, is subject to question.

Case 2 has been previously reported.[9]

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BARBITURATE POISONING TREATED BY PHYSIOLOGICAL METHODS

WITH OBSERVATIONS ON EFFECTS OF BETA, BETA-METHYLETHYLGLUTARIMIDE AND ELECTRICAL STIMULATION

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• *Barbiturate poisoning was treated in 243 patients, of whom 160 were comatose on admission to the hospital and 18 required mechanical respirator. The state of the reflexes was at times a confusing criterion of the depth of poisoning. The immediate danger was generally respiratory; the patient's airway was cleared scrupulously, and every step taken to insure adequate intake of oxygen. The circulatory management, in deeply comatose patients, included the starting of venoclysis at the time of admission to provide an immediate route if plasma expanders or vasopressor drugs became necessary. The four patients who were not saved all proved to have serious underlying medical problems in addition to the barbiturate poisoning. Their histories are given with four others to illustrate various principles of treatment. Hemodialysis used in one of these cases removed 890 mg. of barbiturates from the circulation of a deeply comatose patient who made a complete recovery. The use of analeptic drugs and electrical stimulation afforded little additional help and did not provide an adequate substitute for the direct physiological treatment of depressed respiration or circulation.*

There is a lack of unanimity on recommendations for the most effective treatment of barbiturate poisoning. The traditional use of pharmacological stimulants in treating patients depressed to the point of coma has been challenged, particularly by Scandinavian workers.[1] New stimulants, alleged to be "barbiturate antagonists," recently have been advocated.[2] Physical methods of stimulation with subconvulsive electrical currents also have been recommended to treat barbiturate poisoning.[3] Queries in the literature [4] have expressed the confusion that has been created for physicians treating patients with severe poisoning.

The ultimate test of a treatment program consists of its therapeutic results. In barbiturate poisoning, the ideal treatment program is that which provides the highest salvage rate among the poisoned, with the least number of serious complications. The less complicated such a program can be made, the more likely it is to be applied widely and effectively. Unfortunately, many existing recommendations for treatment in barbiturate poisoning are based on studies in so few patients that no valid conclusions can be drawn about the value of the specific treatment recommended. It can be said, however, that, in any large series to date, the mortality rate among patients in coma from barbiturate poisoning who have been treated with analeptics has been higher than among comparable subjects treated without central nervous system stimulants.[1]

The present paper reviews the treatment of 243 consecutive patients with barbiturate poisoning. One hundred sixty patients were comatose on admission to the hospital, and 123 of these were severely depressed. The use of analeptics and other methods of general stimulation was omitted from the routine care of these patients. Selected studies were performed on seriously depressed subjects, however, to evaluate further the potential therapeutic value of a recently introduced pharmacological stimulant as well as the value of electrical stimulation. There were many patients with severe poisoning: 18 required treatment in a mechanical respirator and 25 required vasopressor agents. There were four deaths, giving a total mortality rate of 1.6% for all patients and of 2.5% for the comatose patients. No incapacitating sequelae were observed among the survivors.

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Classification and Evaluation

Subject Material.—All patients with acute barbiturate poisoning admitted to the King County Hospital, Seattle, between Aug. 1, 1953, and Nov. 1, 1956, were included in this study. The age, sex, and depth of coma for all patients are given in figure 1. Patients were classified according to depth of poisoning roughly according to the grouping of Reed and co-workers.[5]

Group 0 was made up of patients who, on admission, could be aroused to consciousness by stimulation and could give their own histories. The patients of group 1 were in coma but withdrew or groaned with moderate "painful" stimuli. Consciousness was usually regained within a few hours of admission. Group 2 contained subjects who were deeply comatose but who grimaced or showed some minimal response to maximal painful stimuli such as vigorous squeezing of the Achilles tendons. Group 3 consisted of subjects who failed to show any response whatsoever to vigorous painful stimuli. Tendon reflexes usually were markedly depressed or absent (see below), and circulatory depression was sometimes present. Group 4 included patients who showed no response to painful stimulation and who remained in deep coma for over 36 hours or had serious respiratory or circulatory depression.

The presence of corneal and stretch reflexes is sometimes cited as differentiating shallow from deep coma due to barbiturate poisoning. While most severely depressed patients in the present series had no detectable corneal reflexes, many who were less severely poisoned and who grimaced readily after painful stimulation also failed to show corneal reflexes. Complete absence of stretch reflexes generally was an indication of deep poisoning, but the converse was not true. That is to say, several patients with detectable or even brisk knee jerks had severe medullary depression with apnea and required artificial respiration. Nine subjects in group 2, three in group 3, and four in group 4 showed hyperactive tendon reflexes, increased resistance to passive stretch of the extremities, ankle clonus, or decerebrate posturing during the early hours of their coma. Most of these signs of spasticity were unaccompanied by clinically evident systemic anoxia. Three subjects demonstrated spasticity in the arms and legs shortly after admission to the hospital, at the same time that vasopressors were required to maintain blood pressure and artificial respiration was being given because of otherwise sustained apnea. It is apparent from the foregoing that the state of the reflexes was often an unreliable guide to the severity of respiratory or circulatory depression in barbiturate poisoning. The following case report illustrates this phenomenon:

Case 1 (F. C., table 1).—A 28-year-old male who was in a hospital ingested 2.9 gm. of pentobarbital sodium with coffee on an empty stomach on Dec. 10, 1953. He rapidly lost consciousness and was in deep coma in 15 minutes. Twenty minutes after ingestion of the barbiturate, before lavage could be initiated, the patient became apneic and was placed in a portable respirator. At the time he had no corneal response or pupillary light reflexes, but knee jerks and ankle jerks were active. Within the next hour his blood pressure gradually dropped, and intravenous administration of phenylephrine (Neo-Synephrine) hydrochloride was started. An endotracheal tube was inserted, gastric lavage was carried out, and the patient was transferred to a tank-type respirator. At three hours it was noted that, although he was still completely apneic, he had bilateral ankle clonus. Over the next 24 hours he developed bilateral Babinski reflexes, spasticity in his lower extremities, and spinal reflex withdrawal to tracheal stimulation, although no spontaneous respiratory motions were present. At no time had he been cyanotic. At 16 hours respiratory movements returned, with a tidal volume of 125 cc. Artificial respiration was continued, however, for two more hours, until the tidal volume reached physiological levels. Phenylephrine was required to maintain blood pressure for 48 hours. By 72 hours, he was awake, alert, fully oriented, and showed no ill-effects. The pathological reflex responses disappeared at approximately 36 hours, and hyperactive tendon reflexes and signs of spasticity disappeared at approximately 40 hours.

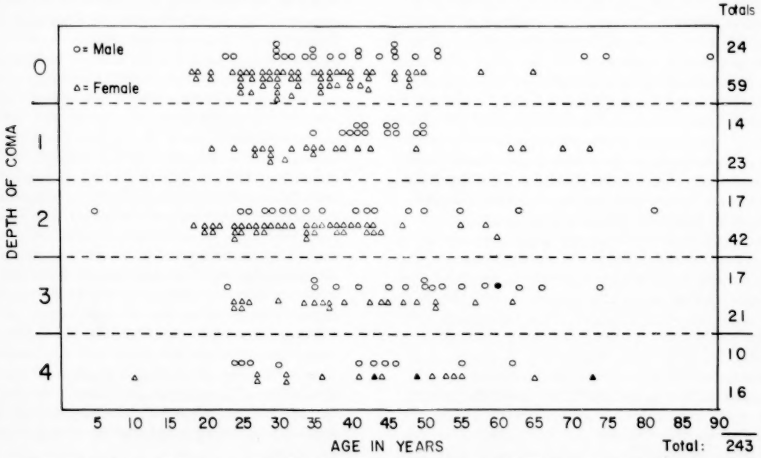

Fig. 1.—Distribution by age in years and depth of coma of 243 patients with barbiturate poisoning. Solid symbols represent deaths.

Blood Barbiturate Levels.—Blood barbiturate levels were determined by the ultraviolet spectrophotometric method [6] in 31 patients. Figure 2 shows the correlation between blood levels of short-acting and long-acting barbiturates and depth of coma observed. There was only fair correlation between blood level and depth of coma. Similar variations have been observed by others [7] and presumably result from differences in individual tolerance (long-time addicts have higher tolerance),

the rapidity of drug absorption (more rapid absorption leading to a deeper coma), the amount of alcohol or other drug consumed with the barbiturate, and the time that has transpired between ingestion of the barbiturate and drawing of blood for analysis. At least 43 of the present patients were known to have been drinking alcohol before or while they consumed the barbiturate. Knowledge of blood level of barbiturate was of limited value in guiding treatment for most patients. Blood analysis was helpful, however, in identifying the etiology of coma of unknown causes and in indicating that coma would be prolonged when high blood concentrations of phenobarbital were found.

Treatment Program

Barbiturates are lethal in one of three ways. 1. They produce coma, the complications of which may be fatal. 2. They depress the neural regulation of blood pressure to the point where homeostasis is lost. 3. They depress the central neurogenic control of respiration to the point where homeostasis is lost. Our treatment program, therefore, consisted of three major phases: the treatment of coma, the treatment of circulation, and the treatment of respiration.

Management of Coma.—Initial evaluation and gastric lavage were carried out in the emergency room, lavage being temporarily deferred if patients showed respiratory or circulatory depression. Comatose patients were admitted immediately to the neurological unit, where they were cared for until they regained consciousness. A special treatment room, similar to those established in other hospitals caring for large numbers of patients with barbiturate poisoning, was equipped with oxygen, intubation equipment, pressor drugs, plasma expanders, and respirators. There was close cooperation with anesthesiologists on difficult problems.

Emergency appraisal evaluated chiefly the patient's state of consciousness, his responsiveness to pain, and the integrity of his airway, respiration, pulse, and blood pressure. Patients who were in no immediate respiratory or circulatory danger and who had ingested the drug within the previous four to six hours had their stomachs lavaged, after which 30 cc. of a saturated solution of magnesium sulfate was left in the stomach. Recently, the magnesium sulfate administration has been omitted. One hundred forty-one patients received lavage. Stomach contents were not analyzed for barbiturates, but frank capsular material was recovered from five comatose subjects. There were four certain complications from lavage: three patients developed laryngospasm, two of whom aspirated stomach contents, and one patient was barely breathing when lavage was started and became apneic as the tube was passed. There were four probable complications of lavage: three subjects were noted to have pulmonary rales after but not before lavage, and one had unexplained upper gastrointestinal hemorrhage six hours after lavage. None of the above complications created more than temporary difficulties in management; all could have been prevented had intubation with a cuffed endotracheal tube preceded lavage.

After initial evaluation of the patient's condition, the airway was cleared scrupulously. Patients were placed head-down and semiprone on a hospital bed that was elevated in the middle and from which the end had been removed to permit immediate, unobstructed access to the face and airway. Subjects in this drainage position were turned from side to side at hourly intervals. Full Trendelenburg positioning was employed for those with hypotension. Blood pressure, respiration, pulse, color, level of consciousness, and urine output were checked at half-hour intervals by nurses or medical students and recorded on special charts. Patients were seen at least hourly by physicians. Those in deep coma were given constant medical supervision. The eyes were protected by mineral oil and, at times, by taping the lids shut. If coma lasted over six hours, an indwelling catheter was placed in the bladder. Patients in grade 2, 3, and 4 coma were placed on prophylactic therapy with penicillin.

Circulatory Management.—Intravenous administration of fluids was started at the time of admission in deeply comatose patients to provide an immediate route if plasma expanders or vasopressor agents became necessary. Fluid intake was maintained at 3,000 cc. or more daily with one liter of saline solution for

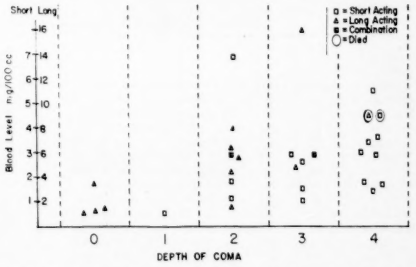

Fig. 2.—Relationship between blood barbiturate level and depth of coma in 31 patients. Type of drug ingested indicated.

most patients. From 20 to 40 mEq. of potassium chloride was added to infusions after the patient's first day of parenteral feeding if urine output was adequate.

Cardiac arrhythmias frequently follow even mild blood pressure drops in experimental animals deeply poisoned by barbiturates.[8] These arrhythmias can be prevented or corrected promptly by administration of pressor agents, which raise mean arterial pressure.[8] For this reason, the indications for pressor agents in human subjects were interpreted liberally. Patients whose systolic blood pressure fell to 85 mm. Hg or less were given ephedrine or methoxamine (Vasoxyl) hydrochloride parenterally to maintain systolic pressure at 90 to 95 mm. Hg or more. Subjects with more severe circulatory depression with weak pulse volume, peripheral cyanosis, tachycardia, or irregularities in cardiac rhythm were given phenylephrine intravenously to maintain adequate systolic pressure levels. If less potent agents failed, levarterenol was employed.

Reliance was placed mainly on pressor agents in managing circulatory problems. Saline solution and water were given intravenously. Blood or dextran was employed only when there was evidence of anemia, hemorrhage, profound shock, or relative refractoriness to chemical pressor agents. Twenty-five patients were hypotensive and were given pressor agents: nine re-

quired no more than 50 mg. of ephedrine or 20 mg. of methoxamine intramuscularly to restore and sustain blood pressure levels of 90/70 mm. Hg or more. Ten patients required either repeated injections of methoxamine or continuous support with phenylephrine or levarterenol for periods lasting several hours. Six subjects had severe circulatory depression: five of these recovered endogenous blood pressure control after requiring levarterenol continuously for from 24 to 96 hours; one was in profound shock on admission to the hospital and died shortly afterwards. Two of the other five patients with prolonged circulatory depression also died, but neither death resulted from the immediate cardiovascular problem and neither patient required pressor agents at the time of death.

Blood was used for four individuals, two of whom had gastrointestinal bleeding. Two subjects required rapid digitalization to counteract pulmonary edema.

Cardiac arrhythmias and tachycardia commonly are reported to complicate severe barbiturate poisoning.[5] In the entire present series there were only three patients with marked tachycardia, which was transient. Electrocardiographic tracings were not done, but there was clinical evidence of significant arrhythmia in only two patients with auricular fibrillation, both of whom had organic heart disease. Pulmonary edema developed at a time of elevated blood pressure in two subjects receiving vasopressor therapy; both responded to reduction of the pressor dose and immediate digitalization. The only other complication of administration of vasopressors was superficial necrosis of the forearm following extravasation of phenylephrine in one patient.

Respiratory Management.—For the most part, respiration was monitored clinically, although alveolar carbon dioxide tensions were studied with a continuous infrared carbon dioxide analyzer in a few patients in deep coma.

The upper airway received immediate attention in all patients. The nose and mouth were repeatedly and thoroughly cleansed with gentle suction, and, if any oral obstruction to breathing persisted, an oral airway was inserted. If stridor did not clear immediately with an oral airway, if there were tracheobronchial rales or evidence of pneumonitis with absent cough reflexes, or if subjects were in deep coma for over 8 to 10 hours, an endotracheal tube was inserted. Tracheobronchial secretions accumulated insidiously. It was common to aspirate large quantities of mucus directly from the trachea of deeply comatose patients who had no signs of respiratory obstruction on chest auscultation. Endotracheal tubes were placed in 22 patients. Six patients, who were in coma for longer than 48 hours, were given a tracheotomy to avoid necrosis of the mucous membranes from the endotracheal tube and to facilitate drainage. Endotracheal tubes otherwise were left in place until vigorous coughing returned; tracheotomies were closed only after consciousness was regained. No complications resulted from maintenance of the airway in the above fashion.

Oxygen was given by nasal catheter at a rate of 4 to 6 liters per minute to many patients in grade 2, 3, and 4 coma. Deeply comatose patients receiving oxygen were closely monitored with the carbon dioxide analyzer. The indiscriminate use of oxygen in those deeply depressed by barbiturates may sometimes produce further depression by carbon dioxide. Barbiturates depress the chemosensitivity of the respiratory center to carbon dioxide. As a result of this, reflex respiratory drives resulting from hypoxia are recruited to stimulate respiration. When there is a depressed center, oxygen therapy prevents anoxemia but permits continued hypoventilation and progressive carbon dioxide accumulation. The following case report illustrates this phenomenon.

TABLE 1.—*Artificial Respiration in Eighteen Patients with Severe Barbiturate Poisoning*

Patient	Age, Yr.	Sex	Drug Ingested, Gm.	Blood Barbiturate Level, Mg./100 Cc.	Respirations/Min.	Cyanotic: Out of Respirator	Cyanotic: In Respirator	Duration of Artificial Respiration, Hr.	Result
R.S.(case 2)	43	M	Pentobarbital sodium, 5.0	5.5	0	Yes	No	20	Recovered
E.B.(case 3)	51	F	Secobarbital sodium, 5.5	5.0	0	Yes	No	45	Recovered
E.G.	41	M	Pentobarbital, 2.4	1.8	0	Yes	No	24	Recovered
T.K.	65	F	Pentobarbital, not known	1.3	0	Yes	No	2	Recovered
R.G.	30	M	Secobarbital, 4.0	...	0	Yes	No	16	Recovered
L.B.	25	M	Pentobarbital, not known	3.4	0	Yes	No	13	Recovered
F.C.(case 1)	28	M	Pentobarbital, 2.9	...	0	Yes	No	22	Recovered
H.B.	44	M	Secobarbital, not known	1.3	16	Yes	No	16	Recovered
J.G.	44	F	Secobarbital, 2.5	...	16	Yes	No	4	Recovered
M.H.(case 5)	43	F	Pentobarbital, not known	...	26	Yes	No	44	Died
R.M.	6	F	Amobarbital, not known	...	14	Yes	No	7	Recovered
N.H.	51	F	Pentobarbital, not known	2.9	24	Yes	No	13	Recovered
P.B.(case 7)	60	M	Phenobarbital, not known	...	20	Yes	Yes	16	Died
G.H.	31	M	Secobarbital, 2.5	3.6	12	Yes	No	2	Recovered
D.D.	33	F	Secobarbital, 2.2; amobarbital, 2.2	...	Not known	Yes	No	2	Recovered
M.M.(case 6)	49	F	Phenobarbital, not known	9.2	26	Yes	Yes	30 min.	Died
K.P.	43	F	Secobarbital, 3.0	...	18	Not known	No	10 min.	Recovered
P.C.	27	F	Secobarbital, not known	2.7	0	Not known	No	5 min.	Recovered

CASE 2. (R. S., tables 1 and 2).—A 43-year-old male was transferred from another hospital on July 8, 1956. He had ingested approximately 5 gm. of pentobarbital 20 hours previously. Therapy at the other hospital had consisted of provision of an endotracheal airway and administration of levarterenol, caffeine, and oxygen (delivered in a tent). His respirations had been shallow at a rate of 24 per minute when administration of oxygen was started, and it was noted that faint cyanosis cleared with oxygen therapy. One hour before his transfer he was observed by a nurse to stop breathing. Artificial respiration was begun immediately with an intermittent positive-pressure ventilator.

On his admission to this hospital, there was no spontaneous respiration and the blood pressure was 85/50 mm. Hg. Corneal, pupillary, and tendon reflexes were absent. There was no response to painful stimuli. A tank respirator was employed to provide artificial respiration, and oxygen was delivered to the endotracheal airway. Two hours later his $pACO_2$ was 57 mm.

Hg (normal 35-40 mm. Hg), and the serum bicarbonate level was 36 mEq. per liter (normal 25-30 mEq.). Intratank pressures were increased, and the $pACO_2$ was reduced gradually to 37 mm. Hg. β,β-Methylethylglutarimide (Methetharimide, Megimide) was given in a dose of 350 mg. over a period of 40 minutes. Spontaneous respiration did not appear (table 2). Artificial respiration was continued until 21 hours after admission and the 41st hour of coma. He awoke on the fourth day. Careful neurological testing demonstrated no evidence of permanent damage. A blood sample obtained at the 20th hour of coma contained 5.5 mg. of barbiturate per 100 cc.

Alveolar carbon dioxide was continuously monitored in 10 other deeply comatose patients receiving oxygen. In only one instance (L. M., table 2) was an elevated carbon dioxide tension found in the expired air in a subject breathing spontaneously. Elevated carbon dioxide tensions otherwise were found only during apnea.

Eighteen patients were treated with artificial respiration (table 1). Seven were apneic either at the time of or shortly after admission and required respiratory support for from 2 to 45 hours before regaining spontaneous, effective breathing. Five patients were breathing feebly but were cyanotic outside the respirator despite endotracheal airways and clear tracheobronchial trees. One man (P. B., table 1) was cyanotic both in and out of the respirator until a plug was removed bronchoscopically from the right mainstem bronchus, and five patients were placed briefly in respirators because they were transiently apneic in the emergency room or appeared clinically to be suffering from hypoventilation.

Evaluation of ventilatory efficiency in patients in deep coma sometimes was extremely difficult. It was clear that completely apneic subjects needed artificial respiration to survive, and patients who were cyanotic unless given artificial respiration also appeared to have definite need of respiratory aid. Shallow breathing without frank cyanosis was more difficult to evaluate. Hypothermia and coma reduce metabolic demands, so that resting ventilation is expected to be low in patients with barbiturate poisoning. Cyanosis is present only when arterial oxygen saturations fall to dangerous levels approximating 80% or less. Oxygen therapy may prevent hypoxemia but fails to assist carbon dioxide excretion in patients with hypoventilation. Direct analysis of arterial blood oxygen and carbon dioxide tensions is too time-consuming to be useful as an immediate guide to treatment. No complications of artificial respiration were encountered in this series. Specifically, there was no indication that respiratory alkalosis was deleterious, and no need for complicated biochemical monitoring was created by the use of respirators. This observation, plus the serious potential danger of anoxia to the nervous system, resulted in the use of artificial respiration if any doubt existed as to the effectiveness of spontaneous ventilation. Because of this liberal employment of respiratory aid, it is possible that the last six patients listed in table 1 received artificial respiration unnecessarily.

For apneic patients, artificial respiration was administered by intermittent positive-pressure ventilators or manually compressed anesthesia bags until transfer to mechanical body (tank-type) respirators was effected. Subjects who were breathing spontaneously but were apparently suffering from hypoventilation were placed directly in the body respirator, usually after passage of an endotracheal tube. Oxygen was given to patients in respirators. Use of the respirator was discontinued only when full spontaneous ventilation was resumed. Mechanical artificial respiration nearly always produces hyperventilation. Because of this, every hour or so the respirator was turned off for approximately two minutes to allow endogenous carbon dioxide to accumulate before it was concluded that continued apnea was the result of drug-induced depression rather than of passive hyperventilation. Two-minute apneic periods do not induce significant hypoxemia in subjects on oxygen therapy. The following case report illustrates the successful treatment of severe barbiturate poisoning by vasopressor agents and artificial respiration.

Case 3 (fig. 3) (E. B., tables 1 and 2).—A 51-year-old woman ingested approximately 3.5 gm. of secobarbital sodium between two and six hours before admission. She was deeply comatose, areflexic, and had no obtainable blood pressure. Her pulse rate was 40 per minute, and respirations declined from 6 per minute to none while she was being examined. Her blood barbiturate level was 5 mg. per 100 cc. An endotracheal tube was put in place, and the patient was put in a tank respirator. From 5 to 8 mg. of phenylephrine per hour failed to raise her

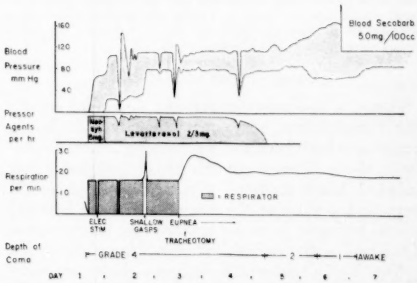

Fig. 3.—Clinical course of 51-year-old woman (E. B., case 3) with severe barbiturate poisoning treated with pressor agents and artificial respiration.

blood pressure above 60 mm. Hg systolic. Electrical stimulation to the legs at 2.5 and 5 ma. failed to initiate respiration or maintain blood pressure. Phenylephrine was replaced by levarterenol, approximately 0.6 mg. per hour being required to maintain adequate blood pressure. Feeble, gasping, spontaneous respiratory movements were observed at 27 hours, but these were ineffective, and she was returned to the respirator until the 43rd hour, when spontaneous breathing returned. Forty-five hours after admission the endotracheal tube was replaced by a tracheotomy. Despite the administration of 3,000 to 4,000 cc. of fluids daily, including whole blood, levarterenol was required to maintain blood pressure until the 86th hour. Corneal and withdrawal reflexes also reappeared at approximately 86 hours. She began to arouse by the 114th hour and regained consciousness on the sixth day. She was found to have a paralysis of the lower part of the brachial plexus on the right, but on the ninth day extensive neurological and psychological testing showed no other neurological or intellectual defect.

Hemodialysis.—Hemodialysis by the artificial kidney is an effective means of clearing barbiturates from the blood.[9] However, the technique of setting up the dialyzing unit is time-consuming and complex. During the hours required to prepare a patient for dialysis, most subjects who have taken a short-acting barbiturate will pass through the critical period of their de-

pression. Dialysis, therefore, cannot substitute for artificial respiration or vasopressors, but it may be valuable by reducing the duration of coma induced by long-acting barbiturates. The following case report illustrates this usage.

Case 4. (W. F., table 2).—A 26-year-old female in the fourth month of pregnancy was admitted on June 3, 1956, after ingesting an unknown amount of phenobarbital. She was in a moderately deep coma at the time of admission, showing rudimentary withdrawal, but within eight hours she became completely unresponsive and areflexic. Her blood pressure was barely perceptible at 90/70 mm. Hg, and her respirations were 26 per minute and shallow. An endotracheal tube was passed, and she was given phenylephrine transiently to bring her blood pressure to 100/60 mm. Hg. Her condition remained stable, but she was still in deep coma, and at 48 hours her blood barbiturate level was "over 20 mg. per 100 cc." A tracheotomy was performed at 72 hours. At 87 hours she was still in deep coma, with a blood barbiturate level of 12 mg. per 100 cc. Blood dialysis was carried out for five and one-half hours by Dr. Belding Scribner and co-workers with a Skeggs-Leonards dialyzer. Dialysis was complicated by hemorrhage of approximately 1,000 cc. around a cannula previously inserted in the femoral vein. During dialysis, 890 mg. of barbiturate was removed by this method and the blood barbiturate level fell from 12 to 8 mg. per 100 cc. It was estimated that an additional 100 mg. (average 10 mg. per 100 cc. concentration) of barbiturate was lost with hemorrhage. At the end of the dialysis she began to respond to pain for the first time since shortly after admission, and she coughed and swallowed spontaneously. Two days later she awoke. She had a spontaneous abortion the next day, but she suffered no other serious complications of prolonged coma.

Complications and Deaths

Sixteen of the surviving patients developed significant complications, some more than one. In seven, lavage may have been the precipitating factor as mentioned above. There were only two complications that outlasted hospitalization: a paralysis of the radial nerve and a palsy of the lower part of the brachial plexus. Ischemic pressure appeared to be the cause of the neuropathy in both instances. One of the above patients had a transient hemiparesis during recovery from five days of deep coma. An additional patient developed a series of generalized convulsions 16 hours after admission, when she was beginning to awaken. There were no other neurological sequelae, and careful neurological testing of all patients prior to discharge revealed no organic mental defects or other motor defects attributable to prolonged coma.

Eleven patients developed bronchopneumonia, usually bilaterally, which cleared in from one to five days of antibiotic therapy. Two patients, only one of whom had been lavaged, had massive hematemesis. One patient developed oliguria for 16 hours after being in profound shock on admission. This same woman developed auricular fibrillation during treatment with levarterenol. Most patients left the hospital between 24 and 72 hours after recovering from coma. No urinary complaints referable to catheterization were registered in that time.

The four patients who died all had serious medical problems in addition to barbiturate poisoning. In retrospect, it appeared that at least one of the four deaths may have been due to an omission of therapy, and another may have resulted from anoxia that was unnecessarily prolonged due to lack of prompt tracheobronchial intubation. Brief protocols of the patients who died follow.

Case 5 (M. H., table 1).—A 43-year-old female chronic alcoholic with hepatic cirrhosis had a portacaval shunt two years previously. She had taken 4.8 gm. of pentobarbital between 24 and 48 hours before admission. She was in grade 4 coma and had extensive early superficial decubitus ulcers over the extensor surfaces of her extremities and sacrum. Her blood pressure was unobtainable. She was cyanotic and had a respiratory rate of 28 per minute. She had atelectasis of the right upper lobe and pneumonitis of the right lower lobe. Her blood pressure was brought to 100/60 mm. Hg with phenylephrine, and she was given oxygen. Cyanosis cleared only after a tracheotomy was done and she was placed in a respirator. She improved, administration of pressor agents and use of the respirator were stopped, and she was responding to vocal stimuli on the seventh day, when she suddenly died. Autopsy showed bilateral bronchopneumonia, acute pulmonary infarction, and diffuse hepatic necrosis.

Case 6 (M. M., table 1).—A 49-year-old female was found on March 15, 1956, in a transient's hotel with empty phenobarbital and diphenylhydantoin (Dilantin) sodium bottles. When she was admitted, her blood pressure was unobtainable, no peripheral pulses were palpable, and she was cyanotic despite a respiratory rate of 26 per minute. Her right arm was macerated and contused, the duration of injury appearing to be over 24 hours. She failed to show a pressor response to methoxamine or levarterenol and died one-half hour after admission while transfusions were being prepared. She had 9.2 mg. of barbiturate per 100 cc. of blood. A coroner's autopsy showed "no evidence of intracranial pathology."

Case 7 (P. B., table 1).—A 60-year-old male was admitted Sept. 17, 1954. He was a chronic alcoholic and had had hypertension for over eight years. He had taken an unknown amount of phenobarbital between 3 and 12 hours before admission. His blood pressure was 180/100 mm. Hg, and he was completely unresponsive. Tendon reflexes were present and equal. During gastric lavage he developed laryngospasm and was shortly afterwards given oxygen and placed in a respirator because of cyanosis, although his respiratory rate was 20 per minute. He remained moderately cyanotic in the respirator. Bronchoscopy was delayed 16 hours, but removal of copious mucus at that time and subsequently through a tracheotomy kept him free of cyanosis and without need of further respiratory aid. On Sept. 24 he had improved markedly and responded to verbal commands, but on Sept. 25 he suddenly died. Autopsy showed an enlarged heart and extensive pulmonary edema.

Case 8 (M. Q., table 2).—A 73-year-old female was admitted April 4, 1956, after ingesting an unknown quantity of pentobarbital. Her blood barbiturate level was 4.3 mg. per 100 cc. Her respiratory rate was 8 per minute, her blood pressure was 70/20 mm. Hg, and she was areflexic and unresponsive to all stimuli. A Babinski reflex was present on the left. She required levarterenol for four days to maintain her blood pressure at levels of 100/60 mm. Hg. Electrical stimuli augmented her ventilation (table 2) but failed to induce coughing or to arouse her. She remained unresponsive and in deep coma, and she developed clinical signs of bilateral bronchopneumonia despite tracheotomy on the third day. After her death on April 12, it was discovered that, due to oversight, antibiotics had not been prescribed at the time of her admission or subsequently. Autopsy showed extensive bilateral bronchopneumonia, pulmonary edema, old rheumatic aortic valvulitis, hemorrhagic ulceration of the duodenum, and a small cerebellar infarct.

Pharmacological and Physical Stimulants

β,β-Methylethylglutarimide.—At the outset of the present study we elected not to use stimulants such as picrotoxin because of their dubious value and potential harm.[1] Our early therapeutic results justified the reliance placed on purely physiological treatment methods. During the course of the present study, β,β-methylethylglutarimide was introduced by Shaw and

co-workers.[2] The original report stated that the drug possessed specific properties of barbiturate antagonism and that it shortened coma. When the drug became available to us, therefore, experimental and clinical studies were instituted with it.

β,β-Methylethylglutarimide was tested experimentally on cats and dogs poisoned with pentobarbital.[8b] The first serious effect of barbiturate poisoning in these studies was respiratory arrest; larger doses of barbiturate produced hypotension and cardiac arrhythmias, ultimately leading to death. Animals treated with artificial respiration and pressor agents survived administration of barbiturates in amounts 6.7 times greater than the dose producing lethal respiratory arrest in untreated animals. β,β-Methylethylglutarimide, however, failed to stimulate spontaneous breathing in animals receiving more than 1.4 times the lethal dose in untreated animals. The drug stimulated a pronounced blood pressure rise in lightly anesthetized animals, but in those in deeper coma the pressor response was less reliable than the response to phenylephrine. Single doses of β,β-methylethylglutarimide sufficiently large to produce muscle twitching and cardiac arrhythmias failed to induce immediate lightening of coma in deeply anesthetized animals. There was no physiological evidence that β,β-methylethylglutarimide specifically antagonized barbiturates. Its properties of central nervous system stimulation appeared similar to but less intense than those of picrotoxin. However, the rapid onset of action of β,β-methylethylglutarimide made it possible to avoid some of the complications of overdosage often observed with picrotoxin.

Controlled observations on β,β-methylethylglutarimide were made in five patients. The drug was given intravenously in 50-to-250-mg. increments at intervals of three to five minutes to a total of 100 to 1,200 mg. (table 2). Two trials of this drug failed to initiate adequate respiration or blood pressure responses in one patient (R. S., case 2), but the other four patients showed increased responsiveness to stimuli within 15 to 50 minutes of treatment. Post-treatment psychotic reactions were not observed. There was little convincing evidence that β,β-methylethylglutarimide shortened coma, although muscle spasms were produced with ease, as was accentuation of stretch reflexes. Others have observed that the drug does not shorten coma or hasten the rate of elimination of barbiturate from the blood.[10]

TABLE 2.—*Effects of β,β-Methylethylglutarimide and of Electrical Stimulation*

Patient	Age, Yr.	Sex	Grade Coma	Drug Ingested, Gm.	Blood Barbiturate Level, Mg./100 Cc.	Effect of β,β-Methylethylglutarimide	Effect of Electrical Stimulation
W.F.(case 4)	26	F	3	Phenobarbital sodium, not known	8.0	After dialysis 90 mg. → coughing, swallowing, increased pain response. Recovered	No effect before dialysis. Effect similar to β,β-methylethylglutarimide after dialysis
L.M.	27	F	3	Secobarbital sodium, not known	Not done	At 2 hr. 200 mg. → general tremor, increased respiration with drop in $pACO_2$ from 49 mm. Hg (high) to 42 mm. Hg (normal). At 7 hr. 200 mg. → spontaneous motion at extremities. Recovered	5 ma. to legs increased respiration. Effect more marked after 200 mg. of β,β-methylethylglutarimide
R.S.(case 2)	43	M	4	Pentobarbital, 5.0	5.0 at 18 hr.	Apneic, with $pACO_2$ 57 mm. Hg. 350 mg. → no respiration at 22 hr. At 28 hr. 350 mg. → spontaneous shallow respiration at 30 min. with climbing CO_2 level. At 42 hr. 300 mg. → deepened respiration. No effect on pain response. Recovered	At 42 hr., 10 and 15 ma. to legs deepened respiration. No effect on absent pain response
A.D.	58	M	4	Secobarbital, not known	Not done	250 mg. → slightly deeper respiration. $pACO_2$ fell from 41 to 37 mm. Hg. Recovered	5 ma. to legs initiated spontaneous respiration when patient removed from tank respirator
J.E.	41	F	3	Pentobarbital, 2.8	4.0	At 1 hr., 550 mg. → increased respiration, $pACO_2$ from 35 to 31.3 mm. Hg, extensor rigidity on painful stimuli, ankle clonus, no arousal. At 4 hr., 550 mg. → extensor spasms, no effect on blood pressure of 86/66 mm. Hg. At 6 hr., 550 mg. → no effect on blood pressure of 82/70 mm. Hg. Required methoxamine. Eventually responded spontaneously at 20 hr.	2.5 ma. increased respiration, dropped $pACO_2$ from 35.2 to 30.2 mm. Hg at 1 hr. No effect on blood pressure of 110/84 mm. Hg
B.S.	25	F	2	Pentobarbital, 2.4	1.0	Not given	5 ma. to legs increased respiration from 18 to 28/min., increased decerebrate posturing. Recovered
M.K.	37	F	4	Secobarbital, 1.0; Pentobarbital, 1.0; alcohol	Not done	Not given	2.5 ma. bitemporally increased respiration from 18 to 21/min., blood pressure from 80/50 to 120/80 mm. Hg, deep tendon reflex from + to +++. No arousal. Recovered
E.B.(case 3)	51	F	4	Secobarbital, 5.5	5.0	Not given	5-10 ma. to legs failed to interrupt apnea or produce blood pressure rise at 8th or 21st hr. Recovered
M.Q.(case 8)	78	F	4	Pentobarbital, not known	4.3	Not given	2.5 ma. bitemporally increased ventilation from 11 to 14.7 liters/min. No arousal or lightening noted after 6 hr. continuous stimulation. Patient later died
T.K.	65	F	4	Type and dose unknown	Not done	Not given	No effect on respiration, circulation, or blood pressure. Recovered

The experimental and clinical data from this laboratory thus indicate that responsiveness to β,β-methylethylglutarimide as a stimulant is inversely related to the depth of narcosis. Both the experimental and clinical data indicate that the drug may supplement, but cannot be substituted for, direct physiological control of blood pressure and respiration in severe barbiturate poisoning. Recent work [11] citing the respiratory stimulating effects of β,β-methylethylglutarimide on seven apneic patients indicates that three patients failed to respond to first infusions of the drug, while in one other subject spontaneous respiration was delayed until 15 minutes after the end of the infusion. Survival, therefore, depended on artificial respiration, not on β,β-methylethylglutarimide. A companion paper from the same hospital [12] states that, of 24 seriously

poisoned patients treated with β,β-methylethylglutarimide, 7 died. The same workers previously had reported a 1.6% mortality in barbiturate poisoning treated by physiological methods and without stimulants.[1b]

Electrical Stimulation.—Nonconvulsive electrical stimulation with electrodes applied both to the head and peripherally has been employed since 1950 in the treatment of clinical barbiturate poisoning.[3] In many of the reported cases, quantitative evaluation of the depth of coma has been difficult to ascertain from published data. The mortality rate of treated patients in series containing more than 20 has ranged from 5 to 11%. Experimental work on the technique has demonstrated that ventilation is augmented by electrical stimulation in poisoned animals already breathing spontaneously but that the response is progressively less with deeper levels of narcosis.[1a] Data from this laboratory indicate that, in cats and dogs, electrical stimulation will not restore spontaneous ventilation in animals receiving more than the respiratory-arrest dose of pentobarbital.[8b] No case of electrical stimulation interrupting apnea in human barbiturate poisoning has been found, although the case of Shanklin and coworkers [3b] suggests that depressed breathing and circulation can be restored to physiological levels by electrical stimulation.

Electrical stimulation was given by a Reiter CW47 stimulator (loaned by Reuben Reiter, New York City) by either cranial or peripheral electrodes to 10 deeply comatose patients in the present series (table 2). All but one patient survived. Currents up to 10 ma. were applied if lesser stimulation produced no desired effect. Two patients (A. D. and E. B., table 2) were apneic when electrical stimulation first was administered: one failed to show any response to two minutes of electrical stimulation; spontaneous breathing began in the other when electrical stimulation was applied and continued after it was discontinued. Two additional nonapneic patients failed to show any respiratory, circulatory, or systemic neuromuscular response to electrical stimulation. All other patients demonstrated increased ventilation after electrical stimulation and some also demonstrated prompt improvement in circulation and reflexes. Arousal was not observed in any patient. Electrical stimulation also was given to a few patients in mild coma. Quantitative observations were not made, but all writhed and groaned when the stimulus was applied. These patients responded in a similar but less pronounced manner to vigorous squeezing of Achilles tendons.

The above observations indicate that electrical stimulation may improve the treatment of moderately depressed patients with barbiturate poisoning by augmenting chest expansion, thereby reducing the risk of pneumonia. By constantly delivering afferent stimuli, it appears possible that electrical stimulation may facilitate the rate at which important reflexes, such as coughing, appear. Electrical stimulation does not appear to be an effective substitute for vasopressor agents and artificial respiration in the severely depressed patient. Certainly, it is not possible to support the recommendation that electrical stimulation, left in the hands of nurses, reduces the need for close supervision by the physician of the patient with barbiturate poisoning.[3a]

Comment

This report supports Nilsson's original contention that excellent results as regards mortality and significant morbidity can be gained by managing severe barbiturate poisoning entirely as a problem of depressed circulatory and respiratory function. The number of patients requiring artificial respiration is larger than previously has been reported. Proponents of stimulants have called programs of the present type "complicated." This is difficult to accept. It was found that the rotating resident physicians and medical students rapidly learned the essentials of the physiological program and administered it effectively. Scrupulous upper airway toilet, careful positioning for pulmonary and oral drainage, adequate hydration, antibiotic administration, and oxygen therapy are familiar to all physicians and well-trained nurses. Giving vasopressor agents by infusion, with the rate of infusion being guided by blood pressure observations, is not difficult. Endotracheal intubation greatly facilitates and improves the management of the deeply comatose patient, and it is urged that all physicians dealing with coma learn to insert an endotracheal tube. Finally, artificial respiration is neither hazardous nor complicated to administer. The tank respirator was chosen to treat most of the patients with severe respiratory depression herein described. This was the choice because cuirass or chest respirators generally provide less ventilation than does the tank. Anesthesia apparatus, or any of a number of positive-pressure-breathing devices or ventilators now available, provide ventilation equal to that of the tank respirator, however, and could readily have been substituted. These might have provided some advantages in ease of nursing care, but they were less familiar to the staff during the time of most of this study.

It is important in the management of the depressed patient to establish optimal therapy immediately rather than to wait for complications and then treat them. Pharmacological and physical methods of stimulation may supplement direct physiological care of the patient but cannot be relied upon as substitutes for artificial respiration and pressor agents.

Summary and Conclusions

Of 243 consecutive patients with barbiturate poisoning admitted to the King County Hospital, Seattle, 160 were comatose and all but 4 recovered. Treatment was directed toward three problems: maintaining physiological circulatory activity, maintaining physiological respiratory exchange, and preventing the complications of coma. Pressor agents and artificial respiration were used liberally to insure circulatory and respiratory homeostasis. Analeptics were not employed therapeutically, but special studies analyzed the effects of β,β-methylethylglutarimide (Methetharimide, Megimide) as well as the effects of electrical stimulation. β,β-Methylethylglutarimide showed little evidence of true barbiturate antagonism but appeared to possess

nonspecific analeptic properties. The analeptic effects were more rapid in onset than those of picrotoxin, and there were fewer undesirable side-reactions. Electrical stimulation to either head or thighs evoked respiratory and other responses in lightly anesthetized subjects, but this method was unreliable in patients in deep coma. Excellent results in treating barbiturate poisoning are gained without employing pharmacological or physical analeptics. No method of general systemic stimulation used in this study provided an adequate substitute for direct physiological treatment of depressed respiration or circulation.

The blood barbiturate level determinations were done by Dr. T. A. Loomis of the Washington State Toxicology Laboratory.

The β,β-methylethylglutarimide used in this study was supplied as Mikedimide by the Panray Corporation, New York.

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CLINICAL NOTES

BETA, BETA-METHYLETHYLGLUTARIMIDE (MEGIMIDE) IN TREATMENT OF BARBITURATE INTOXICATION

REPORT OF A CASE

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and
J. Weldon Bellville, M.D., New York

In 1954, Shaw and co-workers [1] introduced a new barbiturate antagonist, β,β-methylethylglutarimide (Megimide). Since then, many reports of its use for the treatment of barbiturate intoxication,[2] activation of the electroencephalogram,[3] and rapid termination of barbiturate anesthesia [4] have appeared in the literature. The most satisfactory results have been obtained in patients who have taken less than 2 gm. of barbiturate and have been in coma for less than 12 hours. Because of the danger of overdosage (vomiting and muscular fasciculation), doses of 1 gm. of β,β-methylethylglutarimide have seldom been exceeded. This drug has been postulated to be either a barbiturate inactivator or a competitor for the same substrate in the brain.

The following case report is presented because of the use of a large dose of β,β-methylethylglutarimide (5.5 gm.) in the treatment of barbiturate intoxication. The electroencephalogram was employed to evaluate the depth of the narcosis and to monitor the recovery after treatment had been started.

From the Division of Anesthesiology, Memorial Center for Cancer and Allied Diseases.

At 11 p. m. of day 0, a 34-year-old woman took 2 gm. of pentobarbital and 1.2 gm. of phenobarbital by mouth. At 8:30 p. m. of the next (day 1) she was admitted to another hospital, where gastric lavage was performed and an endotracheal tube was introduced. The blood pressure was sustained with an arterenol (Levophed) bitartrate drip. The patient also received amphetamine (Benzedrine) sulfate and intravenously given fluids, but her condition did not progress satisfactorily, and she was transferred to Memorial Hospital for Cancer and Allied Diseases 57 hours after the barbiturate consumption. At this time, the patient was still receiving an arterenol drip, the blood pressure was 80/50 mm. Hg, and the pulse rate was 120 beats per minute. During the night she had received 10 mg. of amphetamine intravenously for a total of 40 mg.

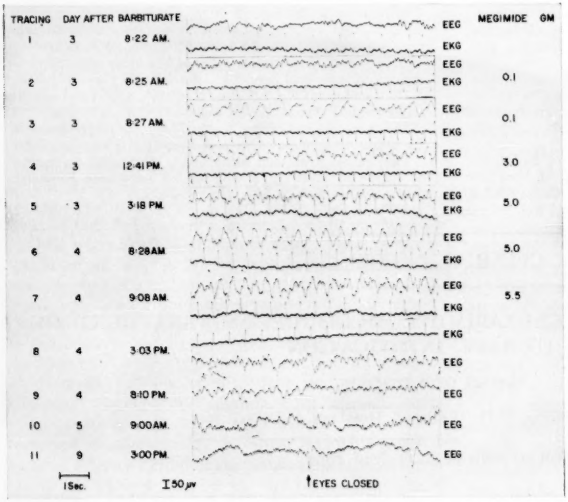
At 8:22 a. m. of day 3 the patient was areflexic; periorbital edema and considerable chemosis were present. An endotracheal tube was necessary to maintain the airway, and the patient coughed very slightly when the trachea was suctioned; the pupils were small and had some reaction to light. The respiration rate was 9 per minute. The patient was being given oxygen

via funnel. The blood pH was 7.22, the serum carbon dioxide level was 22 mEq. per liter, and the pCO_2 was 51.5 mm. Hg. The electroencephalogram showed level 3 of barbiturate narcosis (see figure, tracing 1, with superimposed electrocardiographic artifacts due to inadvertent pickup of the electrocardiographic complex by the electroencephalograph). This consisted of a two-second interval of quiescence followed by low-voltage bursts of 6 to 8 cps activity.

At 8:23 a. m. the initial dose of 50 mg. of β,β-methylethylglutarimide was injected, and by 8:25 the patient had received 100 mg. of the drug. At this time the electroencephalogram appeared lighter, and there was no burst suppression (see figure, tracing 2). At 8:27, sinusoidal waves began to appear at a frequency of 1 cps, with superimposed fast activity of 10 cps (see figure, tracing 3). At 8:31, after a total of 150 mg. of β,β-methylethylglutarimide had been given, the respiration rate was still 9 per minute but the respirations were deeper in volume. The pulse rate was 120 per minute, and the blood pressure was 84/? mm. Hg. At 8:52 a. m., after 300 mg. of β,β-methylethylglutarimide had been given, the patient was swallowing and reacted vigorously to tracheal stimulation; the respiration rate was 14 per minute, the blood pressure was 78/? mm. Hg, and the pulse rate was 120 per minute. The patient was lacrimating. At this time, the arterenol drip was discontinued, and the blood pressure remained stable. At 10:15 a. m., after 1,000 mg. of β,β-methylethylglutarimide had been given, blood pressure was 84/54 mm. Hg, the temperature was 100 F (37.8 C), and the respirations were 10 per minute and very deep. The electroencephalogram showed a dominant frequency of 2 cps, with superimposed fast activity of about 12 cps. The blood content of oxybarbiturates was 122 mcg. per milliliter, the blood pH was 7.36, the serum carbon dioxide content was 29.6 mEq. per liter, and the pCO_2 was 51 mm. Hg.

At 11:33 a. m., after 2 gm. of β,β-methylethylglutarimide had been given, the patient had an eyelid reflex and moved in response to painful stimulation. The vital signs were otherwise unchanged. The electroencephalogram at this time was similar to that after 1 gm. of β,β-methylethylglutarimide had been given. Antibiotic therapy was started. At 12:13 p. m., after 2,500 mg. of the drug had been administered, the blood content of oxybarbiturate was 124 mcg. per milliliter. At 12:41 p. m., after administration of 3,000 mg. of β,β-methylethylglutarimide, the vital signs were unchanged but there appeared to be an increased fast activity superimposed on the still dominant slow frequency (see figure, tracing 4). At 12:53, after 3,150 mg. had been given, the patient developed horizontal nystagmus. There was no change in the electroencephalogram at this time. At 2:06 p. m., after administration of 4 gm. of β,β-methylethylglutarimide and 50 ml. of 50% dextrose solution, the electroencephalogram remained essentially unchanged. At 3:15 p. m., a lumbar puncture revealed a cerebrospinal fluid pressure of 130 mm. H_2O and crystal-clear spinal fluid.

At 3:18 p. m., after 3,000 mg. had been given, the administration of β,β-methylethylglutarimide was discontinued because there was no further change in the electroencephalogram or the clinical picture of the patient (see figure, tracing 5). At 8 p. m. (day 3) the endotracheal tube was changed, and at that time the larynx was noted to be quite edematous. At 11:30 p. m. a tracheostomy was performed. At 8 a. m. on the fourth day after barbiturate ingestion, the pulse rate was still 110 to 120 beats per minute. At 8:28 a. m. of day 4, an electroencephalographic tracing was taken that showed high-voltage slow activity of 2 cps, with a superimposed electrocardiographic artifact (see figure, tracing 6). At 8:29 a. m., therapy with β,β-methylethylglutarimide was begun again and continued until 9:08 a. m., at which time 500 mg. had been injected. At this time the patient had bilateral Babinski reflexes, but the deep tendon reflexes were still depressed. The electroencephalogram still showed a basic frequency of 2 cps, with an electrocardiographic artifact and possibly an increase in the 10-cps activity (see figure, tracing 7). At 10 a. m. the blood level of oxybarbiturate was 180 mcg. per milliliter.


TRACING
DAY AFTER BARBITURATE
MEGIMIDE GM
1 3 8:22 AM. EEG EKG
2 3 8:25 AM. EEG EKG 0.1
3 3 8:27 AM. EEG EKG 0.1
4 3 12:41 PM. EEG EKG 3.0
5 3 3:18 PM. EEG EKG 5.0
6 4 8:28 AM. EEG EKG 5.0
7 4 9:08 AM. EEG EKG 5.5
8 4 3:03 PM. EKG EEG
9 4 8:10 PM. EEG
10 5 9:00 AM. EEG
11 9 3:00 PM. EEG
1 Sec.
150 μv
EYES CLOSED

Electroencephalographic and electrocardiographic tracings of patient in deep barbiturate narcosis before and during treatment with β,β-methylethylglutarimide (Megimide).

At 10:20 a. m., 50 ml. of 50% dextrose solution was injected intravenously, and the patient opened her eyes both spontaneously and on command. She responded very vigorously to painful stimulation, her respiratory rate was 14 per minute, her blood pressure was 100/60 mm. Hg, and her pulse rate was still between 110 and 120 beats per minute. The electroencephalogram at this time showed slow 1-to-2-cps activity, but when the patient was aroused this pattern would change, so that the basic frequency was approximately 9 cps (see figure, tracing 8). At 3:10 p. m., 50 ml. of 50% dextrose solution was given intravenously, and at 3:14 the pattern still showed occasional 2-cps activity, with a good amount of 8-to-9-cps activity. At 8:10 p. m. (day 4), the electroencephalogram was essentially unchanged (see figure, tracing 9).

On the fifth day after barbiturate ingestion, at 9 a. m., the electroencephalogram showed increased fast activity, with minimal slow activity still present (see figure, tracing 10). At this time, the temperature was 101.6 F (38.7 C), the pulse rate was 135 per minute, and the blood pressure was 120/80 mm. Hg. The patient became more restless throughout the day but still was in a state of narcosis. On the sixth day after barbiturate consumption, the patient was able to talk with her friends, although haltingly. At 9 p. m. of that day, the pulse rate had slowed down to 100 per minute and the temperature was 99.6 F (37.7 C). The patient had her first recollection of her stay in the hospital on this day. On the eighth day the patient was able to talk coherently and discuss current events. However, she was unable to maintain her equilibrium and required support to walk. The electroencephalogram taken at this time showed an essentially normal pattern (see figure, tracing 11). The same day the patient reported the amount of sleeping pills she had taken. She was discharged two weeks after admission to this hospital in good condition.

Comment

The differentiation of barbiturate narcosis from other types of coma is important for therapeutic reasons. The presence of barbiturates in the blood, gastric contents, or urine often cannot be determined immediately. The electroencephalographic pattern of barbiturate narcosis has been described and is the same for barbiturates, thiobarbiturates, and nitrogen-substituted barbiturates.[5] An electroencephalographic tracing showing burst suppression (level 3) is fairly characteristic of deep barbiturate narcosis and, if observed, will aid in the diagnosis of barbiturate intoxication. The electroencephalogram may also be valuable in monitoring the response to treatment.

In this patient, a level-3 pattern of barbiturate narcosis was observed on the initial electroencephalographic tracing. Treatment with β,β-methylethylglutarimide resulted in clinical improvement with concomitant change in the electroencephalogram. When the electroencephalogram failed to improve despite continued treatment with β,β-methylethylglutarimide, it was decided that the therapeutic effect of the drug had been reached at that time, and its administration was discontinued.

The large dose of β,β-methylethylglutarimide given, 5,500 mg., did not produce signs of overdosage either clinically or electroencephalographically (spiky pattern). The cause for the increase in the blood oxybarbiturate level from 125 mcg. per milliliter on day 3 to 180 mcg. per milliliter on day 4 is not at once apparent. Similar observations have been reported by Lous,[6] and an explanation may be found in the work of Butler and Wadell,[7] who showed that undissociated barbiturate is absorbed into the brain, while the dissociated barbiturate remains largely in the plasma. An equilibrium is established between the plasma and the brain barbiturate concentrations. Increasing the plasma pH increases the dissociated barbiturate and shifts this equilibrium, so that the plasma barbiturate level increases and the brain barbiturate level decreases. This may explain why the patient was more responsive even though the oxybarbiturate level of the blood had increased. The concomitant lighter electroencephalographic pattern probably reflected a reduction in the brain barbiturate concentration. Thus, it is possible to have a lighter electroencephalographic pattern in the face of an increased plasma barbiturate level if the brain barbiturate level is decreased.

Summary

A patient who had been in deep barbiturate narcosis for 57 hours was given 5,500 mg. of β,β-methylethylglutarimide (Megimide). There were no signs of overdosage of this drug. The electroencephalographic pattern changed from deeper to lighter level, and the circulatory and respiratory depressions were corrected.

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Dr. John H. Burns of Goldwater Memorial Hospital performed the barbiturate determinations.

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Anxiety Neurosis.—Under the stimulus of stress, the normal intellectual and emotional mechanisms of the stable personality come to the rescue, with ultimate satisfactory resolution of the situation by an integrated effort. In the presence of a deepseated defect of personality or character structure, however, anxiety may find expression in an incapacitating illness attended by physical as well as abnormal psychological manifestations. The victim of an anxiety neurosis, in his resistance to the problems and responsibilities of life, may exhibit a wide range of abnormal reactions, including excessive irritability, hyperactivity, agitation, depression, phobias and hypochondriacal symptoms. Evidences of neurotic or even psychotic tendencies may have been part of the life pattern of some patients from an early age; in others the fundamental difficulty may be so slight that abnormal reactions appear only in the presence of severe stress. . . . An individual's vulnerability is determined in part by constitutional factors of which little is known, and in part by his emotional development as influenced by the environment.—G. L. Usdin, M.D., Use of Promazine in Psychiatric Practice: An Early Study, *Journal of The Louisiana State Medical Society*, July, 1956.

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DIAGNOSTIC AND THERAPEUTIC X-RAY EXPOSURE AND LEUKEMIA

GUEST EDITORIAL

William Dameshek, M.D.
and
Frederick W. Gunz, M.D., Boston

The recent comprehensive reports on the effects of ionizing radiation published almost simultaneously by the National Academy of Sciences in the United States and by the Medical Research Council in England [1] have inevitably led to a reassessment of the hazards of present-day diagnostic and therapeutic x-ray procedures. There has already been some comment in THE JOURNAL on the subject, although the matter of leukemogenesis was not particularly stressed.[2] It can be stated that, of the various etiological factors proposed for leukemia in human beings, the only one that appears to be rather conclusively established is that of ionizing radiation.[3] The evidence for this includes (*a*) the incidence of leukemia in radiologists, which is 8 to 10 times as great as that in physicians in other fields [4]; (*b*) the incidence of leukemia in those surviving the atomic blasts near the hypocenters of Hiroshima and Nagasaki, which is 12 times as great as that in survivors at the periphery of the blasted areas [5]; (*c*) the relatively high incidence of leukemia in individuals in Britain and Holland treated for spondylitis by x-ray [6]; (*d*) the development of leukemia in individuals treated for enlarged thymus by x-ray [7]; and (*e*) the possible leukemogenic effects on the baby of the making of x-rays of the pregnant woman's abdomen to determine fetal size and position.[8] In addition, there are the numerous experiments in animals, including those showing the leukemogenic effects of x-rays and nuclear radiation.[9]

All available statistics indicate that the incidence of leukemia has shown a striking increase in the past 20 years. This was apparent well before the recent increasing use of radioactive isotopes, atomic bomb tests, etc. Is it possible that one of the reasons for this increase is the great expansion in the use of diagnostic and therapeutic x-ray procedures during the last few decades?

Skin Doses of Radiation Received During Common Diagnostic Procedures†*

Part Examined or Procedure	Kv.	Ma.	Time, Sec.	Distance, In.	Radiation Received, r
Chest, anteroposterior	72	200	0.1	72	0.05
Chest fluoroscopy	...	...	...	...	0.7-1.2
Spine, lumbar					
Anteroposterior	55	100	1.5	36	1.5
Lateral	78	50	6	36	5.7
Pelvis	60	100	1	36	1.1
Pregnancy					
Anteroposterior	67	125	2	30	3.6
Lateral	78	50	6	30	9.0
Kidney, ureter, bladder	62	100	1	36	1.2
Gastrointestinal series, per film	78	125	0.4	36	0.65
Gastrointestinal series, total per 6 films	...	...	...	...	4.0
Gallbladder	74	125	0.4	36	0.6
Skull, anteroposterior or lateral	54	100	1.5	36	1.3
Fluoroscopy	75	5	...	As close as possible	0.28/sec.

* With 0.5 mm. Al filtration.
† Data from Handloser and Love: Radiology **57**:252-254 (Aug.) 1951.

Some of the commonly used diagnostic x-ray procedures and the number of roentgens ordinarily supplied may be cited (see table). It should be noted that a lateral x-ray of the spine will supply 6 to 9 r and that a gastrointestinal series with careful fluoroscopy may expose an adult to as much as 20 r. The dosage of x-rays delivered to the abdomen to demonstrate the position of the fetus may be up to 15 r. Even diagnostic x-rays of the teeth must now be observed with much more attention. It has been estimated [10] that in taking a full-mouth x-ray up to 300 r will be delivered to the jaw and that in the angulation procedures to obtain pictures of the lower teeth a considerable x-ray dosage may be delivered to the upper chest. In children receiving regular orthodontic care, it has been customary to take full-mouth x-rays twice annually and skull films once or twice a year. Some persons have full gastrointestinal series every year (20 to 40 r), and, if

From the Blood Research Laboratory, a unit of the Ziskind Laboratories, New England Center Hospital, and Tufts University School of Medicine, and aided by grants from the American Cancer Society, Inc., and the U. S. Public Health Service.

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the patient should perchance go to clinics and hospitals for the same ailment, there is no telling how many x-ray studies will be done.

X-ray therapy for non-neoplastic disease is used far more frequently than one realizes; for example, in such conditions as skin disease, subdeltoid bursitis, rheumatoid spondylitis, or indolent infections. People in the larger cities and in the higher economic brackets are usually in an "exposed" position as regards these specialized therapeutic procedures; this is particularly true if they are of the neurotic, apprehensive type. In studying patients with leukemia, a not uncommon finding is a history of x-ray therapy, usually for skin disturbance. A recent patient had been given four sets of x-ray treatments for relatively trivial ailments in the course of the previous 10 years. A course of x-ray therapy over the skin for one or another form of dermatitis may deliver 1,000 to 1,200 r [11]; for subdeltoid bursitis, 390 r [12]; and for rheumatoid spondylitis, several thousand r.[6] Although the effect of the radiation dosages mentioned will depend not only on the amount of radiation administered but also upon the size and position of the area irradiated and the quality of the radiation used, it is clear that not inconsiderable quantities of radiation may be received by individual patients during single diagnostic or therapeutic procedures.

The data from Hiroshima indicate that a single relatively large dose of radiation may eventually result in clinically evident leukemia. Little is known of the leukemogenic effect of repeated smaller doses, but it would be unwise to dismiss them as unimportant at this stage. It is also essential to bear in mind the latency of leukemogenesis: from three to six years were required in Japan between radiation exposure and the appearance of leukemia, and about the same period between radiotherapy of spondylitis in Britain and Holland and the onset of leukemia.

It is certainly by no means proved that the various diagnostic and therapeutic x-ray procedures cited above are clearly related to leukemia in human beings. Nor is it clear how such exposure might lead to leukemia. It may be that exposure to ionizing rays represents only one factor or the "trigger" mechanism activating some other more fundamental etiological factor, perhaps a virus. Whatever the exact explanation may be, there can be no question that it is now essential not only to raise the yellow light of caution but to go even further. In line with proposals in both the British and American reports, the following suggestions are therefore made.

First, there should be strict reevaluation and eventual limitation of the use of x-rays in treatment of non-neoplastic dermatological disorders and such conditions as bursitis, rheumatoid spondylitis, and enlarged thymus in infancy. This would naturally require the setting up of committees by various medical society and specialty groups. Second, unnecessary and frequently repeated diagnostic x-ray procedures should be limited. Many of these procedures are routine and at times seem to be carried out solely for the sake of completeness of the examination. Many neurotic persons or diagnostic "problem" cases go from clinic to clinic, and each clinic almost invariably feels impelled to take its own sets of x-rays. Whether and how to limit these diagnostic procedures is a matter for individual physicians, clinics, hospitals, and medical societies to discuss. Third, and finally, each diagnostic and therapeutic x-ray procedure should be recorded in a suitable booklet to be kept by everyone as a permanent record of his x-ray dosage. This booklet could tell the doctor at a glance whether the patient was beginning to exceed his lifetime quota of permissible x-ray dosage and, through its psychological effect, would tend to curtail the use of possibly unnecessary diagnostic and therapeutic procedures.

The incalculable value of diagnostic x-ray procedures in saving human life and lessening suffering will probably never be fully assessed, and we do not, of course, suggest limiting of such procedures when they are clearly indicated. However, it must be said that, in common with many other diagnostic laboratory procedures, x-ray studies are probably used too enthusiastically at times and without much thought as to a possible harmful effect, on either gonads or blood-forming organs. This becomes a particular problem with the present high sandards of medical care and the equally high economic standards of the American public. Together, these two circumstances have led to such a multiplicity of diagnostic and therapeutic measures that it behooves us at this time to pause and reflect, particularly in the case of diagnostic and therapeutic procedures, upon the following questions: 1. Are the procedures essential? 2. Are they being carried out by well-trained and qualified personnel? 3. Is the person in question getting close to his lifetime radiation dosage allowances?

It must be admitted that, even in heavily irradiated individuals, the occurrence of leukemia is relatively uncommon, but, with the leukemia rate going up steep-

6. Footnote 1*b*, appendix B. Van Swaay, H.: Aplastic Anaemia and Myeloid Leukaemia After Irradiation of Vertebral Column, Lancet **2**:225-227 (July 30) 1955.

7. Simpson, C. L.; Hempelmann, L. H.; and Fuller, L. M.: Neoplasia in Children Treated with X-rays in Infancy for Thymic Enlargement, Radiology **61**:840-845 (June) 1954.

8. Stewart, A.; Webb, J.; Giles, D.; and Hewitt, D.: Malignant Disease in Childhood and Diagnostic Irradiation in Utero: Preliminary Communication, Lancet **2**:447 (Sept. 1) 1956.

9. Upton, A. C.; Furth, J.; and Christenberry, K. W.: Late Effects of Thermal Neutron Irradiation in Mice, Cancer Res. **14**:682-690 (Oct.) 1954.

10. Nolan, W. E., and Patterson, H. W.: Radiation Hazards from Use of Dental X-ray Units, Radiology **61**:625-629 (Oct.) 1953.

11. Crawford, G. M.; Luikart, R. H., II; and Tilley, R. F.: Roentgent Therapy in Acne, New England J. Med. **245**:726-728 (Nov. 8) 1951.

12. Witt, C. M., and Titterington, P. F.: Roentgen Therapy in Bursitis of Shoulder: Analysis of 50 Cases Using Both Deep and Superficial Techniques, J. Missouri M. A. **48**:870-873 (Nov.) 1951.

ly decade by decade, serious thought must be given to measures limiting one possible etiological factor, namely, that of x-ray exposure.

ACHALASIA

Achalasia is defined as failure to relax on the part of the cardiac "sphincter"; this term has replaced the older term, cardiospasm, in Standard Nomenclature of Diseases and Operations. The patients usually complain of dysphagia but may or may not have spasmodic substernal pain. They gradually become emaciated. The cause of this condition is unknown, but in these patients ganglion cells of the myenteric plexus in the lower portion of the esophagus are absent and the neuromuscular mechanism of the esophagus is disturbed. The disease may occur at any age but is relatively rare in patients under 30. Although emotional factors may aggravate the condition, there is no evidence that such factors have ever caused it.[1] It has been experimentally produced in cats by a high vagotomy.[2]

In patients with achalasia the diagnosis is often not made at once. It is important, however, to establish the diagnosis and especially to rule out malignancy before undertaking corrective measures. Many drugs have been tried to relieve this condition, including amyl nitrite, octyl nitrite, methantheline, epinephrine, levarterenol, phentolamine, phenoxybenzamine, and tetraethylammonium chloride. Hightower [1] found such drugs in general to be of no value. Matzner and Windwer [3] reported symptomatic improvement after the use of oxyphenonium bromide in eight patients, all of whom had had previous treatment with such conventional means of treatment as diet and dilatation. They were careful to add, however, that this should be used as an adjunct to conventional medical management. Although a bland high-protein high-caloric diet is usually prescribed and avoidance of very hot or very cold foods is advised, diet plays a relatively unimportant part in the treatment of achalasia.

Brown [3] states that where water will pass a string will pass and recommends passing all bougies or dilators over a string to avoid perforation of the redundant esophagus. Although some observers report good results with the use of unguided dilators, most authorities find such means ineffective and in some instances, if undue pressure is applied, hazardous. Different types of balloon dilators can be distended with air, water, or mercury. The amount of dilating pressure that can be exerted on the cardia increases with the density of the medium used. Vinson [4] states that one dilatation with a hydrostatic dilator gave complete permanent relief in 75% of his patients. The remaining 25% were improved by one treatment but required further dilatation. In his opinion operation is rarely required, because failure to obtain relief by means of hydrostatic dilatation indicates that the dilator was not maintained in proper position when being distended. Palmer [5] admits that statistical reports favor the use of hydrostatic and metal dilators but still prefers the pneumatic type as being safer and effective in most cases. He believes mercury dilators to be of little value. Although dilatation does not cure the underlying condition, it creates a patulous esophagogastic opening through which food passes by gravity.

Schindler [6] has described a new dilating technique, which he calls brusque dilatation and which appears to accomplish excellent results in the most refractory cases. He carefully rules out not only cancer but also cicatrization, because the clinical findings in patients who have a scar with a spastic overlay may closely similate those of achalasia. In Schindler's series of 84 patients, excellent results were obtained in 80. Two of the remaining four obtained partial relief. There were no deaths, no recurrences, and in most patients one treatment was all that was needed. The method cannot be considered entirely without danger, however.

Of the various operations that have been used to correct this condition, linear incision (Heller's operation) is the best but is rarely indicated. Like most operations for achalasia, it may be followed by a very troublesome esophagitis with or without ulceration, stricture, or shortening of the esophagus. Merendino and Dillard [7] advocate the replacement of the cardiac sphincter with a segment of the jejunum for patients in whom esophagitis has developed as a result of previous surgical treatment, but this operation has not been used widely enough or long enough for a final evaluation to be made. Because the results of nonsurgical treatment when properly applied are so good, it should be given a prolonged trial, especially since there is no relation between the duration of the condition and the percentage of cures obtained.

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2. Brown, C. H., and Albright, C. P.: Achalasia of Cardia and Mega-Esophagus: Report of Five Representative Cases, Cleveland Clin. Quart. **23:**186-199 (July) 1956.

3. Matzner, M. J., and Windwer, C.: Cardiospasm: Favorable Results with Anticholinergic Medication, Am. J. Gastroenterol. **25:**454-462 (May) 1956.

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ORGANIZATION SECTION

FULL SPEED AHEAD!

Dwight H. Murray, M.D.

If I were a singer, I might begin by singing "Happy Birthday." But since I am not, let me extend birthday greetings and congratulate the Council on Industrial Health on its 20th anniversary of outstanding service to the medical profession, industry, labor and the community.

Today you are in the spotlight, not simply because it is your 20th anniversary, but, more important, because industrial health has become one of the most vital services influencing the health of the American people. How and why has industrial health gained this place of importance and influence? Let's take a quick look. Let's see what has developed in industrial health almost entirely within our lifetime—at least within my lifetime, anyway.

Development of Industrial Medicine

Aside from a few early Greek and Roman contributions to industrial medicine, it was Bernardino Ramazzini who in the 17th century foresaw the great future in industrial health and who tried to stimulate the profession's interest in this new field of medicine. His contributions have rightly earned him the title of "Father of Industrial Medicine."

However, Ramazzini's teachings, while they have proved to be sound and while they were copied and paraphrased for years, unfortunately were little practiced during the century following his death. It wasn't until the rise of industrialism and the development of modern biological and medical sciences starting late in the 18th century that industrial medicine began slowly to make progress, first in England. And it was not until the early part of the 20th century that the number of industrial medical investigations and the contributions to industrial health literature amounted to anything in America.

Just after 1910 the U. S. Bureau of Mines started its inquiries into employment conditions. The First National Conference on Industrial Disease under the sponsorship of the American Association for Labor Legislation was called. The National Safety Council was founded, and the first American books on the subject of industrial health made their appearance.

Suddenly the whole field of industrial medicine had become alive with activity. The next few years were extremely significant ones for industrial medicine. The American Medical Association organized its Section on Hygiene and Preventive Medicine in 1915 and held a symposium on industrial hygiene and medicine at the San Francisco meeting. The next year the American Association of Industrial Physicians and Surgeons was formed, and the federal government enacted the important workmen's compensation law.

World War I itself gave industrial medicine great momentum as the cry went up for fewer industrial accidents and less absenteeism. There was war work to be done, and industry and the public called upon medicine and science to hold down accidents, absenteeism, and disease. Originally, of course, industrial medical departments had cared for the injured worker only, but it had become apparent that industrial medical services had also to provide protection against occupational disease, and industrial medical programs had to include preemployment and other physical examinations, health education, counseling, and research.

Industrial health developments of the 1920's and the 1930's were numerous and valuable. There were new books and journals, scores of industrial disease investigations, new laws and new organizations. Undoubtedly, one of the most important events was the organization of the A. M. A. Council on Industrial Health in 1937. The new council—realizing that the health and physical and mental well-being of the industrial employe must be promoted—concerned itself with industrial disease and the health of the worker, with standards of industrial medical practice, with the establishment of committees on industrial health within state and county medical societies and with all programs designed to meet the challenges in the increasingly important field of industrial health.

These then are the highlights in the development of industrial health in the United States up to the creation of the A. M. A. Council on Industrial Health. The history lesson has been short, but that's the kind I always liked.

Recent Progress

The achievements of industrial medicine in the last few decades indicate amazing progress—brought about through the cooperation of physicians, their medical allies, industrial leaders, and labor. It is a remarkable story of successes in the control of industrial diseases and the promotion of health in behalf of the worker, management, and the community.

Specifically, the health hazards of dusts, vapors, gases, fumes, liquids, extremes of atmospheric pressure and temperature, and operations involving repeated motion and vibration have largely been overcome. Encouraging success also is being realized in the prevention of harmful effects of noise.

President, American Medical Association.

Read before the 17th Annual Congress on Industrial Health, Biltmore Hotel, Los Angeles, Feb. 5, 1957.

Heavy metal poisoning, dermatitis, and silicosis have been markedly reduced as have ill health effects from the manufacture and use of solvents and other chemicals. And now medical science has undertaken the large task of preventing harmful health effects from radiation where atomic energy is used.

Industrial medicine also is making a noteworthy contribution to the worker through discovering signs of health impairment and advising consultations with the family physician in instances where indicated. This has played an important role in the early detection and cure of such nonoccupational diseases as TB, cancer, diabetes, emotional disorders and heart and vascular disease. It has led the way in rehabilitating workers and it has championed the cause of the handicapped and older worker. As Dr. Rutherford Johnstone has said: "All this is a far cry from finger-wrapping and insurance medicine."

The safety record, in which industrial medicine has played no small part, is equally striking. In the 15-year period from 1940 to 1955 there occurred a 30% decline in accidental death rates in industry. And the National Safety Council now reports that an all-time low was set in 1955 for the average accident frequency rate for employes in industry.

Records for man-hours worked without a disabling injury are equally astonishing. In its 1956 "Accident Facts" the Safety Council lists the record for man-hours without an accident in a steel company as 8 million! In an automobile factory the record is more than 15 million man-hours, and in a chemical plant it is 28½ million! It is now a fact that most work places are safer than the home and the highways. The worker's lifespan now equals that of the general population.

There have been scores of other triumphs in industrial medicine, too, but time does not permit me to mention them all—I could, but I'm afraid we'd all be here far into the night. All these achievements have rightly placed you in the industrial, medical, and community spotlight.

Today, industry is demanding more medical service, guidance and advice than ever before, and the rapid increase in the number of industrial health physicians is proof of this. Twenty-five years ago there perhaps were only several hundred physicians doing industrial medical work. Today they are estimated at more than 25,000—5,000 full-time, 10,000 part-time, and another 10,000 on-call.

Industries—both large and small—realize that industrial health departments can help them and their employes. For example, a National Association of Manufacturers' survey reports that a well-conducted medical program can reduce accident frequency, occupational disease, labor turnover, absenteeism, and compensation costs by as much as 30 to 40% in most cases and as much as 60% and more in others. No wonder the American Management Association says that "the medical dollar produces more than any other dollar spent by industry."

I don't believe it is pure selfishness on the part of industry, either. I think that most industrialists realize that a worker's environment must never be the cause of ill health or disability.

As a result of this belief and of industrial health programs, the worker has been helped to better health, longer life, steady employment, regular weekly income, higher morale, and a score of other blessings.

Industry and worker are not the only ones who have benefited from industrial health programs. The family and the community have come in for their share, too. Without question, the healthy, happy worker is a better family man and a better citizen of his community.

Like Dr. Shepard, I see modern industry and the modern community as inseparable. As Dr. Shepard has said, "the community literally becomes industry in the person of every worker who goes through the plant gates when working hours begin. Industry becomes the community as each employe goes home." This oneness of industry and community therefore assures the community of direct benefits from industry's medical programs. The industry-worker-family ties also are direct and important, and a benefit to one is a benefit to all.

The rise of industrial medicine has given the local, private practitioner a new role in medicine, too. Today almost every physician, with the possible exception of a few specialists, is directly or indirectly concerned with industrial health. As I stated earlier, already there are 25,000 doctors who have some official medical tie-in with industry—full-time, part-time or on-call.

No longer can any physician look askance at industrial medicine, for all of us are either dealing with it or soon will. If I may be permitted to use a little Navy vernacular here, let me say that the shakedown cruise for industrial medicine is over. Your work in the prevention of occupational disease, job placement, health education and counseling, and research has proved extremely worthwhile.

You also have familiarized your colleagues with the great responsibilities and possibilities of industrial medicine, and you have set the course well. So I say, "full steam ahead for industrial medicine!"

New Challenges

Before I close I would like to make one plea. Community doctors are needed to direct, on a part-time basis, the industrial health programs in the smaller and medium-sized plants, in which the majority of workers are employed. These plants are beginning to call for the services of physicians, but the supply of physicians specializing in industrial medicine obviously cannot meet the demand.

What is needed, particularly for the smaller plants, are part-time physicians who, while not specializing in, are interested in, industrial medicine—its reparative, preventive, and constructive phases. Needed are physicians who can and will provide medical guidance for both management and labor, who can represent both fairly and impartially, and who can grow with industry in the present age of medical, sociological, and technological change.

From my own knowledge and experience I can guarantee that work in prevention of illness will be as satisfying as diagnosis and treatment of disease and injury. In this present age of prevention and protection of health, I see occupational health as a field of most exciting possibilities.

It bears repeating that the physician does not have to be an industrial medical specialist to serve in industry part-time. As long as he is well-trained, is respected in his community, and has a high sense of medical ethics, he is qualified. Attendance at short courses, reading of industrial medical periodicals, and attendance at scientific meetings such as this one will provide him with new information and ideas on how to help management and labor with the occupational health problems ever growing in magnitude and complexity.

I have so characterized these problems because they involve the whole man, including his body, his mind, emotions, temperament, reactions, interests, capabilities, handicaps, personality, and habits.

The problems also must reckon with the changing atmosphere of American industry—its increasing mechanization and use of new production methods and energy sources. They must further reckon with the increasing population of workers—young and old, male and female in every state of the nation.

At every turn in industrial medicine there are new challenges, new opportunities. So let's all make the most of industrial health's bright future and move with full speed ahead!

FEDERAL MEDICAL LEGISLATION

First Session, 85th Congress

Tax Deferment for Retirement Plans and Life Insurance

Representatives Jenkins (R., Ohio) and Keogh (D., N. Y.), in H. R. 9 and H. R. 10, have introduced identical bills that would permit the self-employed individual taxpayer, in computing income tax, to deduct from the adjusted gross income (on self-employment income) 10% of the net earnings from self-employment or $5,000, whichever is less, if used for payments by him each year to obtain retirement income for himself or payments to his beneficiary or his estate. The total deductions allowed could not exceed $100,000 during the taxpayer's lifetime.

For persons between the ages of 50 and 70, in addition to the maximum deductions permitted, an additional 10% of the above formula could be added for each year over age 50. Retirement deposits would be deductible if paid to a restricted retirement fund operated by a bank or into a life insurance company plan providing for annuity, endowment, or life insurance contract or a combination of these, but not for term insurance. Under this plan periodic payments made to the taxpayer after age 65 or to his beneficiary would be treated as ordinary income for tax purposes. Provision is made for the right to borrow from deposited funds or to withdraw them prior to age 65 or to allow for a lump payment at age 65. For these privileges there is a slight tax penalty above that provided for when periodic payments are made at maturity.

Congressmen Coudert (R., N. Y.), in H. R. 45, Keating (R., N. Y.), in H. R. 251, and Ray (R., N. Y.), in H. R. 380, have introduced identical bills that would permit both employed and self-employed taxpayers to deduct from their adjusted gross income a maximum of $3,000 annually or 5% of such income for the self-employed, whichever is less. For employees the maximum is $3,000 or 2½%, whichever is less. More liberal deductions are permitted for persons between the ages of 50 and 70. Funds from retirement plans once entered into could not be payable until the taxpayer becomes 65, unless he becomes permanently and totally disabled prior to reaching such age.

Congressman Coudert (R., N. Y.) in another bill, H. R. 43, would provide that in calculating income tax, "Premiums paid during the taxable year on any annuity or life insurance contract upon the life of the taxpayer shall be allowed as a deduction from gross income to the extent that such premiums do not exceed 10 per centum of the taxpayer's adjusted gross income." All the preceding bills were referred to the Committee on Ways and Means.

Problems of the Aging

Representatives Coudert (R., N. Y.), in H. R. 44, and Ostertag (R., N. Y.), in H. R. 373, would establish a commission to study and report findings and legislative recommendations in problems of the aging. The fact-finding commission would be appointed by the President, the President of the Senate, and the Speaker of the House of Representatives. The field to be covered would include such subjects as care and services in the home, foster home facilities, recreation centers, institutional facilities for chronically ill, and employment and retirement programs. These measures are similar but not identical. H. R. 44 was referred to

From the Washington Office of the American Medical Association.

the Interstate and Foreign Commerce Committee, and H. R. 373 was referred to the Committee on Education and Labor.

Representative Rodino (D., N. J.), in H. R. 396, has introduced a measure that would establish a commission on old age and retirement benefits, appointed as in H. R. 373 and H. R. 44. This commission also will report its findings and recommendations to Congress. This bill was referred to the Ways and Means Committee.

Bureau of Older Persons

Representative Rhodes (D., Pa.), in H. R. 383, would establish a Bureau of Older Persons within the Department of Health, Education, and Welfare and authorize federal grants to states to develop and carry out plans for the benefit of the older population. Two million dollars would be authorized to develop such plans and 2 million dollars for fiscal year 1958, 3 million dollars for fiscal 1959, 4 million dollars for fiscal 1960, and 5 million dollars for fiscal 1961 to assist the states to initiate and carry out the projects promulgated as above. This bill was referred to the Committee on Education and Labor.

Veterans' Legislation

Veterans' Benefit Act 1957.—Representative Teague (D., Texas) proposes in a 224-page bill, H. R. 53, "To consolidate into one Act, and to simplify and make more uniform, the laws administered by the Veterans' Administration relating to compensation, pension, hospitalization, and burial benefits, and to consolidate into one Act the laws pertaining to the administration of the laws administered by the Veterans' Administration." He makes no major changes in the present laws except to permit military personnel, retired with ailments or injuries service-incurred in peacetime to obtain hospital benefits without going through the procedure of obtaining a compensation award as they are now required to do.

Veterans' Compensation Act 1957.—Representative Teague (D., Texas), in H. R. 54, would "simplify and make more nearly uniform the laws governing the payment of compensation for service-connected disability or death." This bill is one part of H. R. 53 and merely codifies the present law as it relates to compensation and presumption of service-connection for certain diseases and disabilities. It continues as in the present law the presumption of service connection for cases of chronic and tropical diseases becoming manifest within one year after separation from active service; active tuberculosis, within three years after separation; and multiple sclerosis and psychoses, within two years after separation.

Veterans' Hospitalization Medical Care and Burial Benefits Act.—Representative Teague (D., Texas), in H. R. 57, would "consolidate all laws administered by the Veterans' Administration which relate to furnishing hospital and domiciliary and medical treatment to veterans, to the acquisition and operation of hospitals and domiciliary facilities, and to burial and funeral benefits for veterans." The material in this proposal is also contained in H. R. 53. It does not change the present laws relating to these facets of veterans' benefits.

Requirements for VA Hospitalization and Domiciliary Care.—Representative Teague (D., Texas), in H. R. 58, would "impose additional requirements on certain veterans seeking hospitalization or domiciliary care in Veterans' Administration facilities." Under the existing law, hospitalization is permitted to veterans with non-service-connected disabilities on a space-available basis if a statement on oath is made by the veteran that he cannot pay for such care. Under present regulations veterans with non-service-connected disabilities are required to sign a 10-P-10 form covering much of the same material that Representative Teague proposes to be required by law. This proposal would require the veteran to declare: (1) all medical, surgical, hospitalization and health insurance, and all annuities, of which the applicant is the beneficiary; (2) all life insurance policies on which the applicant makes premium payments, and all life insurance policies which are paid in full on which the applicant has made premium payments; (3) the value of all property, real and personal, owned by the applicant, and of the extent to which such property consists of cash, bank accounts, and United States Savings Bonds; (4) The average monthly net income received by the applicant during the preceding six-month period from all sources; (5) the average monthly expenditures of the applicant; and (6) a statement of the applicant's net worth (being a statement of total worth minus outstanding legal obligations)."

After the applicant makes the above declaration, "the Administrator of Veterans' Affairs shall determine the type and extensiveness of the medical care and treatment, if any, that is necessary for the applicant, and the probable period of the applicant's hospitalization. In the case of an applicant who is determined to require less than thirty days' hospitalization and who does not require emergency care or treatment and is not suffering from tuberculosis or a psychosis, the Administrator of Veterans' Affairs shall before such applicant makes the statement under oath: (1) determine, approximately, what it would cost the applicant at another institution in the area, to obtain care and treatment comparable to that deemed necessary for the applicant by the Administrator of Veterans' Affairs; (2) review with the applicant the declaration . . . (3) tell the applicant the approximate cost of such care and treatment at another institution in the area as is deemed necessary for him by the Administrator of Veterans' Affairs." (4) read to the applicant the section of veterans' laws providing for forfeiture of all veterans' benefits and a possible fine and imprisonment for making false affidavits, declarations, state-

ments, etc. (38 U. S. C. 715); and the section from the U. S. Criminal Code (12 U. S. C. 1001), which provides a fine of not more than $10,000 or imprisonment, or both, for falsifying, concealing, or covering or making false, fictitious, or fraudulent misrepresentations or statements in connection with dealing with any U. S. government agency.

Hospitalization for Combat Veterans.—Representatives McDonough (R., Calif.), in H. R. 329, and Rodino (D., N. J.), in H. R. 389, have introduced identical measures that provide that "Any veteran who engaged in combat with the enemy in active service with a military or naval organization of the United States during some war, campaign, or expedition, who applies to the Administrator of Veterans' Affairs for hospitalization for a disease or injury which he claims was incurred or aggravated in combat service, shall be immediately admitted to a Veterans' Administration facility for such hospitalization pending a determination under this Act of whether or not such disease or injury was so incurred or aggravated. Hospitalization furnished by reason of this paragraph shall be furnished without charge therefor."

Service-Connected Disabilities.—The following measures dealing with service-connected disabilities have been introduced.

Neuropsychiatric Ailments: Congressman Ray (R., N. Y.), in H. R. 381, has introduced by request a bill that would provide that "the Administrator of Veterans' Affairs shall furnish at Veterans' Administration hospitals or by contract with State hospitals to all persons discharged or released from active service, under conditions other than dishonorable, who have service-connected disabilities, necessary hospital and medical care for any neuropsychiatric ailments which they have, whether or not service connected."

Leprosy: Representative Rogers (R., Mass.), in H. R. 413, would increase from one to three years after discharge from military service the period of presumption of service-connection for leprosy.

Chronic and Tropical Diseases: Representative Rogers (R., Mass.), in H. R. 415, proposes to make a similar increase (from one to three years) in the period of presumption of service-connection for chronic and tropical diseases.

Presumption for Malignant Tumors: Representative Thompson (D., N. J.) has introduced a measure, H. R. 420, that would "provide that malignant tumors developing a 10 per centum or more degree of disability within two years after separation from active service shall be presumed to be service-connected." All the preceding veterans' bills were referred to the Veterans' Affairs Committee.

Insurance

Emergency Hospital Care for Spanish-American War Veterans.—Representative Rogers (R., Mass.) by request has introduced a measure, H. R. 418, that would authorize emergency hospital care for veterans of the Spanish-American War, including the Boxer Rebellion and the Philippine Insurrection, when emergency hospital care is needed incident to outpatient treatment. Outpatient treatment is at present authorized without regard to whether such illness or accident was the result of military service. This bill was referred to the Veterans' Affairs Committee.

Noncancelable Insurance.—Representative Christopher (D., Mo.), in H. R. 116, proposes "to prohibit insurance companies doing insurance business of an interstate character from issuing group health, hospitalization, and accident insurance which may be canceled after a period of three years for any reason other than nonpayment of premium." This measure was referred to the Interstate and Foreign Commerce Committee.

Health Insurance Pooling.—Representative Thompson (D., N. J.), in H. R. 489, proposes waiver of antitrust laws to allow small insurance companies (writing less than 1% of the total health insurance) and voluntary plans to pool assets to guard against individual losses with experimental types of health insurance coverage. This does not provide a government-operated reinsurance fund. The proposal seeks priority in the development of prepayment protection "(1) against the heavy costs of long and expensive illness, which can so easily lead to financial catastrophe; (2) for retired and other older persons, for whom there is increased likelihood of expensive long-term illness. (3) for persons who, because they live on farms or in other sparsely populated areas or are not associated through their employment with readily insurable groups, are difficult to reach through present enrollment methods; and (4) for persons already suffering from physical impairments."

Benefit Plans in Lieu of Social Security.—Representative Curtis (R., Mo.), in H. R. 131, proposes "to encourage by use of private benefit plans in lieu of social security by providing that individuals" who provide private benefit or retirement plans for themselves will not be required to pay social security taxes or entitled to the social security benefits. The private benefit plans would have to be at least equal to the Old Age and Survivors Insurance benefits to which the individual would be entitled, the cash surrender value of the private plan would have to be at least equal to the payroll taxes they would have paid to OASI. If the individual ceases to participate in the private plan, the equivalent of the OASI taxes would have to be paid into the OASI retirement fund. The bill was referred to the Committee on Ways and Means.

Tax Exemption

Unlimited Tax Deductions for Medical Expenses.—Representative Curtis (R., Mo.), in H. R. 129, proposes to remove the maximum limitation on allowances for deductions for medical and dental expenses in computing income tax. The present law permits not more than a $2,500 deduction per person for a taxpayer and his dependents, with a maximum of $10,000

annually. The $2,500 figure per person would not change, but the $10,000 maximum would be removed. This bill was referred to the Ways and Means Committee.

Medical Expense Credit on Tax.—Representative Keating (R., N. Y.), in H. R. 286, would permit a taxpayer in calculating his income tax to subtract from his income tax (not his gross income) the amount paid by him during the taxable year for health insurance. The amount deductible would vary according to his adjusted gross income: "(1) If the adjusted gross income of the taxpayer is $2,000 or under, 90 per centum of the amount paid; (2) If the adjusted gross income of the taxpayer is between $2,001 and $4,000, 85 per centum of the amount paid; (3) If the adjusted gross income of the taxpayer is between $4,001 and $6,000, 80 per centum of the amount paid; (4) If the adjusted gross income of the taxpayer is between $6,001 and $8,000, 75 per centum of the amount paid; (5) If the adjusted gross income of the taxpayer is between $8,001 and $10,000, 70 per centum of the amount paid; and (6) If the adjusted gross income of the taxpayer is $10,001 or over, 60 per centum of the amount paid." This bill was referred to the Ways and Means Committee.

Tax Credit for Education Expenses.—Representative Thompson (D., N. J.), in H. R. 490, would amend the Internal Revenue Code to allow a deduction against the individual income tax (not gross income) of 30% of the amount paid during the year to institutions of higher education for tuition or fees for himself or any other individual. This was referred to the Ways and Means Committee.

Department of Civil Defense

Representatives Dollinger and Farbstein (D., N. Y.), in H. R. 147 and H. R. 174, respectively, have introduced identical bills that would establish within the Department of Defense a "Department of Civil Defense" to which would be transferred the functions of the Federal Civil Defense Administration: "The Secretary of Defense shall make such studies and investigations, and adopt such regulations as are consistent with existing law, and recommend to the Congress whatever legislation is required (1) to authorize the Department of Civil Defense to be supplied necessary personnel through normal civil-service procedures or, to the extent that the same may be deemed necessary and feasible, through Selective Service induction procedures, (2) to authorize and direct the Secretary of the Department of Civil Defense to prepare comprehensive and effective programs of civil defense, and (3) to authorize the Secretary of Civil Defense to make known to the public to the fullest possible extent, consistent with the national security, the facts about the destructive power of weapons and other instruments of modern warfare and the most effective means of coping with the dangers thereof and protecting persons and property against them." This bill was referred to the Armed Services Committee.

Limiting the Effect of Treaties

Representative Burdick (R., N. D.), in H. R. 194, would provide "That no treaty now existing or to be hereafter negotiated shall in any way abridge the sovereign power of the United States or of any States, nor shall such treaty change, amend, or abridge any law of the United States or of any State in the United States." This was referred to the Foreign Affairs Committee.

Sanitation Facilities and Services for Indians

Representative Judd (R., Minn.), in H. R. 246, proposes to authorize the surgeon general of the Public Health Service to conduct surveys until June 30, 1961, as to the need for sanitary facilities and measures and to develop projects for the construction of such facilities among the Indian population. The Indian tribes would be encouraged to assume or share in the responsibility for the construction and operation of the facilities. The measure states, "The Surgeon General shall consult with, and encourage the participation of, States and political subdivisions thereof, and the government of the Territory of Alaska in carrying out the provisions of this Act." This was referred to the Interior and Insular Affairs Committee.

Federal Aid for Nurse Education

Representative Lane (D., Mass.), in H. R. 306, would provide a program of grants for scholarships to encourage education and training in the field of nursing. He would authorize matching grants to the states not to exceed 50% of the cost of (1) assisting the schools of nursing in maintaining and increasing the enrollment and to improve and expand their curriculums and (2) to provide for scholarships to defray part or all of the cost of tuition, books, equipment, and maintenance. The surgeon general would administer the program and would conduct a campaign to attract young men and women to the field of professional and practical nursing. This was referred to the Interstate and Foreign Commerce Committee.

Registration and Reporting of Welfare and Pension Plans

Representative Thompson (D., N. J.), in H. R. 487, would require the registration of pension and welfare plans covering 25 or more persons. Welfare plans would include medical, surgical, or hospital care or benefits and disability, death, and unemployment benefits. Pension benefit plans are those that provide insurance or annuity contracts. Plans that cover more than 100 persons would be required to file an annual report giving in detail, expenses, salaries, fees, reserves, etc.

The Labor Department, to which such reports would be made, would have broad investigatory powers and whenever it appeared the law were be-

ing violated or embezzlement were present, the Labor Department could transmit such evidence to the Attorney General for the purpose of instituting criminal proceedings. This bill was referred to the Committee on Education and Labor.

FDA STATEMENT ON STEM-TYPE PESSARIES

In a formal policy statement published in the Federal Register, Feb. 12, the Food and Drug Administration concluded that "stem-type and wing-type intracervical and intrauterine pessaries are dangerous to health, and regardless of their labeling, may be shown to be misbranded." Distributors were advised by the FDA to remove such articles from the interstate market at once, with a strong hint that otherwise court proceedings would be instituted. The FDA emphasized that its action does not apply to other types of pessaries, which are safely used following surgery and for supportive purposes.

The policy statement declares that it is now the consensus of medical opinion among experts qualified by scientific training and experience to evalute the safety of such devices that stem-type and wing-type intracervical and intrauterine pessaries are dangerous for use under any form of labeling and serve no useful purpose.

Dr. Albert H. Holland Jr., medical director of the Food and Drug Administration, said that such devices have been used as contraceptives for many years but are not reliable for preventing pregnancy. He said that the pessaries have been labeled for use only under medical supervision since 1941 and that the decision to institute legal action against them was reached as a result of a recent medical survey in which 92% of the experts consulted regarded these devices as dangerous for use under any conditions. These opinions were supported by many known cases of injuries, infections, cancer, and pregnancy associated with the use of such pessaries.

MEDICINE AND THE LAW

RULE OF "RESPONDEAT SUPERIOR"

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The rule of *respondeat superior* today has wide application. Therefore, for the purpose of this article, the discussion of its effect will be confined to the area of professional liability of physicians resulting from the acts of partners, assistants, technicians, and employees.

The Meaning and Development of "Respondeat Superior" in the Law

Possibly the best way to approach a subject such as this would be to inform the reader of the meaning of the term *respondeat superior*, the reasoning involved in it, and its development, all of which play an important role in the practice of medicine. Just what does the term *respondeat superior* mean? It might briefly be explained in a short phrase that is often used—let the master answer. This maxim means that a master is liable in certain cases for the wrongful acts of his servant and a principal for those of his agent.[1]

An understanding of what is meant by a servant might clarify the significance of the cases to follow. The court of civil appeals of Texas defined a servant as follows:[2]

> . . . it must appear from the evidence that such other person was the employee of the defendant, over whose actions in the premises defendant had dominion and control; or that the defendant, being called upon to do the work, directed it to be done by such other person, under circumstances which would justify an ordinarily prudent and reasonable person in believing that such other person was aiding the defendant in his professional work; or that defendant held out to the public that the other dentists in his office were his assistants, and that plaintiff, believing and relying upon such representation, presented himself at the defendant's office to have his tooth extracted, and submitted himself to one of such employees in the defendant's office, relying upon the defendant and not upon the individual who extracted the tooth, as the responsible head of the business.

As to the question of reasoning or logic behind such a rule Lord Chief Justice Best in *Hall* v. *Smith*[3] stated: "The maxim of respondeat superior is bottomed on this principle, that he who expects to derive advantage from an act which is done by another for him, must answer for any injury which a third person may sustain from it." This reasoning has been followed by the American courts.[4]

Other explanations for this maxim of *respondeat superior*, by which the master must respond in damages for injuries inflicted by a servant in the course of employment, have rested upon a great variety of grounds and theories.[5] Representation or agency has been frequently suggested as an explanation of this maxim.[6] The actual reasoning that the courts use in the application of this doctrine is that the agent or the employee becomes the agent of the employer, the individuality of the employee being identified with that of the employer.[7]

The court of civil appeals of Texas in 1935, in the case of *Shell Petroleum Corporation* v. *Magnolia Pipe Line Co.*,[8] expressed the following opinion:

> [The master's] liability for the failure of his servant to exercise the requisite care is founded on his right of control and superintendence over such servant and the duty imposed upon him in the management of his own affairs, whether in person or by employees, to conduct the same so as not to injure another. The

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act of the servant within the scope of his employment must therefore be considered to be the act of the master, for which he is liable to the same extent as if he had performed such act in person 39 C. J. P. 1282, Sec. 1471.

It seems that today the basic reasoning behind this rule has not changed to any great extent, although the courts have used various lines of reasoning in their attempt to explain the result reached. Today, the explanation that is possibly the most widely accepted is best summed up by the statement that the whole doctrine has its foundation or origin in consideration of public policy, convenience, and justice.[9] This idea of justice is felt by many of the courts to be best served by making the master responsible for the injuries caused by his servant acting in the master's service.[10]

It is thought by some and has also been argued before the courts that it is a hard rule, which fixes liability on the employer when the employee has passed out of sight and control, but the courts feel it rests upon a public policy too firmly settled to be questioned. Many of the courts in discussing this rule have stated that it is elemental that every person in the management of his affairs shall so conduct them as not to cause an injury to another. If he undertakes to manage his affairs through others, he remains bound so to manage them that third persons are not injured by any breach of legal duty on the part of such others while they are engaged upon his business and within the scope of their authority.[11]

Possibly the reasoning behind this doctrine and the rationale of its supposed undue hardship upon the employer has been best explained in *Dansey* v. *Richardson*,[12] in which the court stated:

. . . the liability of masters for the acts or omission of their servants weighs heavily on them; but the hardship would be at least equal if the master were not liable; and it would be attended with injustice too. If the master be morally innocent, so must the injured party be also; for he cannot recover, if by his own misconduct or negligence he has contributed to the loss: and, of two innocent persons, surely he should suffer, through whom it is, by the employment of another, the mischief has been occasioned.

The Supreme Court of Oklahoma, in 1923,[13] quoted *Baker* v. *Chicago, P. and St. L. R. Co.* (90 N. E. 1057) as follows: "The maxim of respondeat superior is founded on the principle that he who expects to derive advantage from an act which is done by another for him must answer for any injury 'which a third person' may sustain from it." The same court also quoted *Farwell* v. *The Boston W. R. Corp.* (4 Metc. Mass. 49) as follows: "This rule is obviously founded on the great principle of social duty, that every man, in the management of his own affairs, whether by himself or by his agents or servants, shall so conduct them as to not injure another; and if he does not, and another thereby sustains damage, he shall answer for it."

The doctrine of *respondeat superior* from the very beginning has been closely associated with the law as pertaining to independent contractors. In some of the earlier cases [14] it was thought that the doctrine of *respondeat superior* applied to the relationship between an employer and an independent contractor, but the authority of these few cases was soon overwhelmed by many decisions setting forth the general rule that an employer is not liable for the torts of an independent contractor or the latter's servants. This rule of nonliability of an employer is based on the theory that the characteristic incident of the relationship created by an independent contractor is that the employer does not possess the power of controlling the person employed as to the details of the stipulated work. It is, therefore, a necessary judicial consequence that the employer shall not be answerable for an injury resulting from the manner in which the details of the work are carried out by the independent contractor.[15]

It might be well to add at this point that physicians are, under most circumstances, considered as independent contractors. This is usually the determination in cases in which the issue as to whether the physician is an employee of a hospital has been raised. The courts generally feel that the master-and-servant relationship does not exist between a hospital and a physician who treats the patient.[16] This is the result of the feeling that a professional man, acting upon his own initiative and without the direction of others, is an independent contractor and not the servant of a master.

Now that an explanation has been given as to what the meaning of *respondeat superior* is, the next question that arises is "when does this doctrine apply and under what circumstances."

The Application of the Doctrine

The Supreme Court of Alabama applied the doctrine of *respondeat superior* in a case in which the plaintiff was seeking to recover damages for an assault and battery alleged to have been committed on her person by an agent or servant of the defendant.[17]

The doctrine of the liability of the master for the wrongful acts of his servant is predicated upon the maxims, "Respondeat Superior" and "qui facet per alium facit per se." In fact, it rests upon the doctrine of agency. Therefore the universal test of the master's liability is whether there was authority, expressed or implied, for doing the act; that is, was it done in the course and within the scope of the servant's employment? If it be done in the course or within the scope of the employment, and in the accomplishment of objects within the line of his duties, the master will be liable for the act. If the servant steps aside from his master's business, for however short a time, to do an act not connected with such business, the relation of master and servant for the time is suspended.

There is no basic or fundamental distinction to be drawn between the liability of a principal for the tortious acts of his agent and the liability of the master for the tortious acts of his servants (25 L. R. A. [NS] 343 and Restatment of the Law of Agency, Sec. 212, etc.).

In both cases, whether master and servant or principal and agent, the liability is founded upon the maxim *respondeat superior*, and, in both cases the liability to be determined by considering the factual standpoint is the question of whether or not the tortious act was done while the agent or servant was acting within the scope of employment.[18]

The foregoing material shows some of the reasoning that has been applied by the various courts throughout the United States upon the subject of *respondeat superior*. Often, however, mere rules and statements are meaningless unless they can be seen in action as applied to various types of actual fact situations. Also, there must be some degree of predictability as to what might result from a set of facts, so that lawyers and other interested parties can have a valuable understanding of a field of law. Thus, it would possibly give an even clearer understanding of this area of the law if we saw how it has been applied in various situations and in various courts in states throughout the United States.

Technician as Employee or Servant

First let us take a situation where the acts of a technician bring this doctorine of *respondeat superior* into operation, because possibly more cases arise involving technicians than any other type of employee or servant. In an Arkansas case [19] an action was brought by a patient against the physician for injuries sustained by the patient while x-rays were being made by a technician employed by the physician. The technician was experienced in the use of x-ray but was not a physician. In this particular case the technician had been instructed by the physician to do a certain procedure and was doing all the work involved. The patient was burned as a result of the x-ray machine's coming in contact with him. The evidence in the case established the relation of master and servant so as to render the defendant physician liable for injury caused by the negligence of the technician. The court made the following interpretation in its opinion.

It is an old and thoroughly established doctrine that, where the relation of master and servant exists, the master is responsible to third persons for injuries resulting from wrongful acts or omissions of a servant within the scope of his employment in the master's service Shearman and Redfield on Negligence, vol. 1, P. 350. A physician is responsible for an injury done to a patient through the want of proper skill and care in his assistant, apprentice, agent or employee 48 C. J. 1137.[20]

The court in its opinion also cited with approval a Pennsylvania Supreme Court decision [21] in which the defendant physician was an x-ray specialist and was held liable for injuries sustained by the negligence of his assistant who was a skilled x-ray technician. In that case it was conceded that the technician was the servant of the physician.

It has been argued in other cases that a skilled and experienced technician should be considered as an independent contractor and not as a servant, but it seems that the majority of the cases overrule this line of argument.[22]

There seems to be little doubt under the law that technicians, nurses, and assistants who are actually employed by the physician can bring about the liability of the physician by their wrongful acts, which are within the scope of their employment. This is especially true in cases in which the employee or servant is actually compensated by the physician or the fact is admitted that such person is an employee or servant.

A situation that has caused some confusion as to whether the doctrine of *respondeat superior* would be applicable is that in cases where nurses, interns, technicians, and assistants are brought into contact with the physician through the medium of a hospital. Most often the question of liability of the physician under *respondeat superior* arises in cases dealing with the acts of nurses who are actually in the employment of either the hospital or the injured patient. In a case in which a nurse failed to read a label on a bottle and handed the wrong medicine to the operating surgeon, which resulted in an injury to the patient, the court said:[23]

A physician is not liable for the negligence of hospital or other nurses, attendants or interns who are not his employees if he has no knowledge thereof, or has no connection therewith, or if it is not discoverable by him in the exercise of ordinary care, or unless he is negligent in permitting them to attend the patient. . . . But it has been held that where a hospital nurse, although not in the regular employ of an operating surgeon, is under his special supervision and control during the operation the relation of master and servant exists, and that the surgeon is liable under the doctrine of respondeat superior for the nurse's negligence.

The above case cited an Oklahoma case in which the patient was burned on the feet and ankles during an operation. In this case a pan of hot water, which was used in wringing out sponges being used in the operation, was placed between the patient's feet. The evidence clearly established that the pan of hot water had caused the injury. It was further brought out that while the nurse was the employee of the hospital she was, nevertheless, during the time required for the actual operation under the direction and control of the operating surgeon and was the servant of the operating surgeon in respect to such services as were rendered by him in the performance of the operation. The court stated: [24]

An examination of the authorities discloses to our satisfaction that the true test of the existence of the relation of master and servant in a given case does not depend upon whether the servant was in the general employ of the master, but upon whether the master actually exercises supervision and control over the servant during the time he uses such servant. A general master may loan the service of his employee to another for a specified purpose and for a short period of time, in which case the individual to whom such general servants are let is the master, and responsible for their negligent acts so long as he exercises actual supervision over them.

A case in which the nurse was held not to be the servant of the operating surgeon is *Clary* v. *Christiansen*.[25] In that case, the patient sued the operating surgeon for injuries resulting from burns caused by an electrical machine. The defendant surgeon had informed the hospital that he wished to use a Davis-Bovie electrosurgical unit and when he arrived at the operating room, such machine was present. While he was in the scrub room, attendants of the hospital removed this machine and replaced it with a Fisher machine, which required a different technique in its use. When the defendant surgeon returned, he did not notice the substitution as the machine had been screened from his view. It seems that the scrub nurse,

an employee of the hospital, was charged with the duty of preparing the room and the instruments and of supplying the instruments to the surgeon during the progress of the operation. The facts further show that the surgeon had no right to direct as to the mode or manner of preparing the room for operation. The court stated,[26] "We are of the opinion that the scrub nurse was not in any sense an employee of the defendant in the task of preparing the room preceding the actual beginning of the operation and that whatever negligence occurred in that connection cannot be attributed to him."

The Supreme Court of Wisconsin held in 1931 that it was a general rule of law that the operating surgeon is not liable for the negligence of interns in the hospitals, but when the intern acts under the surgeon's immediate direction he assumes responsibility for the intern's conduct.[27] A case to the contrary is *McConnell* v. *Williams*.[28] In this case the negligent act that caused the injury was due to an intern's negligent use of silver nitrate in a baby's eyes. The court stated,[29] "The only legal question involved is whether the doctrine of respondeat superior applies, that is to say, whether, for the purpose of and during the course of the operation, which included the immediate caretaking of the infant child, the intern was, in view of the law, the servant or employee of defendant." In this case the physician had specifically requested this particular intern to aid him, and the court held that a jury might find under these facts that the intern had become his temporary servant or employee for the purpose for which he was so engaged. The court further stated: [30]

> If, then it be true that defendant had supervisory control and the right to give orders to the interne in regard to the very act in the performance of which the latter was negligent, it would follow, according to the classical test of agency hereinbefore stated, that a jury would be justified in concluding that the temporary relationship between defendant and the interne was that of master and servant, and that consequently defendant was legally liable for the harm caused by any negligence on the part of the interne.

As we have seen above, the principal ground for holding the physician not liable would be that the wrongful act was performed by someone who was not found to be either a servant or an employee of the physician.

Another situation that gives rise to a defense of the liability imposed by the doctrine of *respondeat superior* is where a principal or employer is sought to be held responsible for the acts of his agent or employee and the agent or employee has been found by the court or jury to be not negligent. In such a case the principal or employer is not liable. Such a case is *Union Painless Dentist, et. al.* v. *Guerra*,[31] in which the jury found that the servant was not negligent or liable but the master was negligent. The court felt that this verdict of the jury was evidently an attempt to shield a servant and find against the master, which, of course, could not be legally done under the laws of Texas. This view, that unless the employee is negligent the master cannot be negligent, is the majority view throughout the United States, with only Kentucky and Montana holding to the contrary.

"Respondeat Superior" and Medical Partnership

Also in line with some of these examples is the question of whether one physician can be held liable for the acts of another physician when the two are practicing their profession under a partnership arrangement. The answer to this question would be 'yes' so long as the physician whose wrongful acts led to the liability was working or acting within the scope of partnership business. The court of civil appeals of Texas [32] stated, "Partners in the practice of medicine are all liable for an injury resulting from the negligence, either of omission or commission, of any one of the partners within the scope of their partnership business."

The functions, rights, and duties of partners in great measure comprehend those of agents, and the general rules of law applicable to agents likewise apply to partners.[33] As a matter of fact, the law of partnership is a branch of the law of agency. Accordingly, the liability of one partner for the act of his co-partner is founded on the principle of agency. The doctrine of *respondeat superior* could then be used, it seems, to further explain the liability of one partner for the negligent acts of another partner. This is based upon the rule that a principal is liable for the acts of his agent, which arises from the rule of *respondeat superior*.

The courts have felt that when physicians and surgeons are in partnership all are liable in damages for the professional negligence of one of the partners, because the act done within the scope of the partnership business is the act of each and all as fully as if each is present and participating in all that is done.[34] But if the partner who causes the damage has, in committing the acts complained of, gone outside the purview of the partnership business, the acts, whether done through wantonness or other motive, will be his own acts and he alone will be responsible.[35]

In the case of *Haase* v. *Morton* [36] the Supreme Court of Iowa was dealing with a case in which two physicians were practicing as a partnership. A patient of one of the partners was allowed to fall down an elevator shaft while in the care of one of the partners after an operation. At the time the patient was under anesthesia and was being taken to his room. Through the neglect of the physician the stretcher was allowed to roll through an open elevator door. The absent partner, in denying his liability for the resulting injuries, contended that whatever liability there was should fall on the doctor who was present at the time of the accident. The court stated that the doctors might assume the duty of returning the patient to his room,[37] "and in such event each member of the firm would be the agent of the other in carrying on the work. It is fundamental that each partner is the agent of the firm while engaged in the prosecution

of the partnership business, and that the firm is liable for the torts of each, if committed within the scope of the agency."

It might be interesting also to set forth a few examples where liability may arise under circumstances where the person considered the servant or employee is himself a physician. Such a case is *Heimlich* v. *Harvey*.[38] In this case the defendant physician contended that he was not liable for the result of treatment given by an associate doctor whom he had employed on a salary-plus-commission basis. The patient received the first treatment from the associate doctor without the patient ever seeing the defendant physician. After the injury resulted, the defendant physician also joined in the treatment of the patient. The Supreme Court of Wisconsin held that the defendant physician had completely acknowledged the acceptance of the physician he had employed to be his own, which is a very good recognition of responsibility under the familiar doctrine of *respondeat superior*.

There are cases that deal with the problem of liability of physicians when two or more are treating the same patient.[39] In these cases it has often been held that one physician may be held liable for the negligent acts of another when such acts are observed by him and he either acquiesced in them or made no attempt to prevent such wrongful acts. This, in reality, does not involve the rule of the previous cases, as the courts are inclined to use the reasoning that the two physicians are joint wrongdoers or tortfeasors, and the courts do not speak in terms of *respondeat superior* as being a basis for the liability.

Changing Interpretation

It has been my aim in this article to further understanding of the legal doctrine known as *respondeat superior* and the ways in which application of that doctrine can result in liability on the part of a physician when he himself has not been at fault but when the actual fault lay with someone who is classified as either his servant or employee. Law, however, like any other subject matter, is in a constant state of change, and one cannot always be sure that the presently accepted doctrine will be the approved doctrine in the years to come. An indication of this change can best be explained by a recent California case, now in the courts, about which a final judgment has not as yet been reached. In the past, it has been fairly uniformly held that physicians, due to the fact that an employer such as a hospital could not control their individual acts, would be classified as independent contractors and as a result the hospital would not be held liable for the wrongful acts of such physicians under the doctrine of *respondeat superior*. This reasoning has been based mainly on the idea that a professional man, acting upon his own initiative and without the direction of others, would necessarily be classified as an independent contractor.[40]

In this case, an anesthesiologist was working under an arrangement with a hospital on a fee-for-service basis. The court held that the anesthesiologist was an agent of the hospital where he did his work thus making the hospital liable for his negligence. In the case, the plaintiff showed that the defendant was one of six anesthesiologists on the hospital staff, that he gave anesthetics for no other hospital, that all drugs and equipment used by him were supplied by the hospital, that he had a regular on-call duty at said hospital, and that a hospital nurse had summoned him to give the anesthetic that resulted in this suit. The court stated: [41]

> It appears that this evidence is sufficient to establish, prima facie, that defendant West was an agent of defendant hospital. There is nothing in the record to show that plaintiff should have been on notice that defendant West was not an employee of defendant hospital and it can not be "seriously contended" that she was obliged to inquire whether each person who attended her in said hospital was an employee or an independent contractor. It follows that the trial court erred in taking the issue of agency from the jury.

Of course, this case has not reached a final conclusion but it does show that there are other lines of reasoning being applied to this area of the law, which could possibly, if sustained, expand the area in which *respondeat superior* is already applicable.

We have seen what the meaning and effect of the doctrine or maxim of *respondeat superior* is and how it is applied in various fact situations. In doing this, I have tried to let the reader see how this doctrine might at some time affect him. Of course, many of the questions in the cases cited here depend upon a particular set of facts. Oftentimes it will be difficult to say with all confidence and certainty that this doctrine will or will not be applied, because each case must stand or fall on its own particular facts, and the final decision must necessarily rest with the judge or jury.

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2. *Wilkins* v. *Ferrell*, 30 S. W. 450, 452 (Ct. of Civil App. of Texas, 1895).

3. *Hall* v. *Smith*, 130 English Reports 265, 267 (1824).

4. *Fetting* v. *Winch*, 104 Pac. 722 (Ore. 1909); *Barker* v. *Chicago P. and St. L. R. Co.*, 90 N. E. 1057 (Ill. 1909); *Gleasen* v. *Salt Lake City*, 74 P.2d 1225 (Utah, 1937).

5. *Kohlman* v. *Hyland*, 210 N. W. 643 (N. D. 1926); *Cochran* v. *Michaels*, 157 S. E. 173 (W. Va. 1931); 18 R. C. L. Master and Servant Sec. 247.

6. *Chase* v. *New Haven Waste Material Corp.*, 150 Atl. 107 (Conn. 1930); *Bray-Robinson Clothing Co.* v. *Higgins*, 276 S. W. 129 (Ky. 1925); *Defoe* v. *Stratton*, 114 Atl. 29 (N. H. 1921).

7. *Mi-Lady Cleaners* v. *McDaniel*, 179 So. 908 (Ala. 1938); *Hoffman* v. *Roehl*, 203 Pac. 349 (Mont. 1921); *Hekman Biscuit Co.* v. *Commercial Credit Co.*, 289 N. W. 113, (Mich. 1939).

8. *Shell Petroleum Corp.* v. *Magnolia Pipe Line Co.*, 85 S. W. 2d 829, 832 (Ct. of Civil App. of Texas, 1935).

9. *(a) Chase* v. *New Haven Waste Material Corp.*, 150 Atl. 107 (Conn. 1930); *(b) Penas* v. *Chicago M. and St. P. Ry. Co.*, 127 N. W. 926 (Minn. 1910); *(c) Higgins* v. *The Waterbliet*

Turnpike Co., 46 N. Y. 23 (N. Y. 1871); *(d) Higbee Co.* v. *Jackson*, 128 N. E. 61 (Ohio, 1930); *(e) Hall* v. *Norfolk and* W. R. Co., 28 S. E. 754 (W. Va. 1897).

10. Footnote 9 *a*. *Hearns* v. *Waterbury Hospital*, 33 Atl. 595 (Conn. 1895).

11. Footnote 9 *a* and *c*.

12. *Dansey* v. *Richardson*, 3 El. & Bl. 143, 164, (Q. B., 1854).

13. *Aderhold* v. *Bishop*, 221 Pac. 752, 755 (Okla. 1923).

14. *Lowell* v. *Boston and L. R. Corp.*, 40 Mass. 24 (Mass. 1839); *Stone* v. *Cheshire Railroad Corporation*, 19 N. H. 427 (N. H. 1849).

15. *Scammon* v. *The City of Chicago*, 25 Ill. 424 (Ill. 1861); *Ciaconi* v. *City of Astoria*, 113 Pac. 855 (Ore. 1911); *Hilsdorf* v. *The City of St. Louis, et al*, 45 Mo. 94 (Mo. 1869).

16. *Norton* v. *Hefner*, 198 S. W. 97 (Ark. 1917).

17. *Hardeman* v. *Williams*, 43 So. 726, 727 (Ala. 1907).

18. Footnote 17. *Stumpf* v. *Montgomery*, 226 Pac. 65 (Okla. 1924). *Merrier* v. *St. Paul M. and M. Ry. Co.*, 17 N. W. 952 (Minn. 1884).

19. *Gray* v. *McLaughlin*, 179 S. W. 2d 686 (Ark. 1944).

20. *Gray* v. *McLaughlin*, 179 S. W. 2d 686, 688 (Ark. 1944).

21. *Kelly et al.* v. *Yount*, 12 Atl. 2d 379 (Pa. 1940).

22. *Wemmett* v. *Mount*, 292 Pac. 93 (Ore. 1930); *Mullins* v. *DuVall*, 104 S. E. 513 (Ct. of App. of Ga., Div. No. 2, 1920); *Ybarra* v. *Spangard*, 154 P. 2d 687 (Cal. 1944).

23. *Hallinan* v. *Prindle*, 62 P. 2d 1075, 1077, 1078 (Dist. Ct. of App., 1st Dist., Cal. 1936).

24. *Aderhold, et al.* v. *Bishop*, 221 P. 752 (Okla. 1923).

25. *Clary* v. *Christiansen*, 83 N. E. 2d 644 (Ohio, 1948).

26. *Clary* v. *Christiansen*, 83 N. E. 2d 644, 645 (Ohio, 1948).

27. *Nickley* v. *Skemp*, 239 N. W. 426 (Wisc. 1931).

28. *McConnell* v. *Williams*, 65 Atl. 2d 243 (Pa. 1949).

29. *McConnell* v. *Williams*, 65 Atl. 2d 243, 245 (Pa. 1942).

30. *McConnell* v. *Williams*, 65 Atl. 2d 243, 246 (Pa. 1942).

31. *Union Painless Dentist, et al.* v. *Guerra*, 234 S. W. 688 (Ct. of Civil App. of Texas, 1921).

32. *Lee* v. *Moore*, 162 S. W. 437, 440 (Ct. of Civil App. of Texas, 1913).

33. *Irwin* v. *Williar*, 110 U. S. 499 (1884); *Union Nat. Bank* v. *Neill*, 149 Fed. 711 (5th Cir. 1906); *Orr, Jackson and Co.* v. *Perry*, 81 So. 150 (Ct. of App. of Ala., 1919); *Stephens, et al* v. *Neely*, 255 S. W. 562 (Ark. 1923); *Lindley* v. *Seward*, 5 N. E. 2d 998 (Appellate Ct. of Ind., in Banc, 1937).

34. *(a) Hess* v. *Lowery*, 23 N. E. 156 (Ind. 1890); *(b) Boor* v. *Lowery*, 3. N. E. 151 (Ind. 1885); *(c) Haase* v. *Morton and Morton*, 115 N. W. 921 (Iowa 1908); *(d)* and *Hyrne* v. *Erwin*, 23 S. C. 226 (So. Carolina 1885).

35. 42 L. R. A. (NS) 785; 16 Ann. Cas. 353.

36. Footnote 34 *c*.

37. *Haase* v. *Morton and Morton*, 115 N. W. 921, 924 (Iowa, 1908).

38. *Heimlich* v. *Harvey*. 39 N. W. 2d 394 (Wisc. 1949).

39. *Hedlund* v. *Sutter Medical Service Co., et al.*, 124 P. 2d 878 (Dist. Ct. of Appeals, 1st Dist., Div. 2, Cal., 1942).

40. Footnote 10.

41. *Seneris* v. *Haas*, 291 P. 2d 915, 927 (Cal., 1955).

MEDICOLEGAL ABSTRACTS

Blood Tests for Alcohol: Experiments Performed in Court.—The defendant was charged with manslaughter and drunken driving in violation of the California penal and vehicle codes. From a judgment of conviction, she appealed to the district court of appeals, 2d district, division 3 of California.

An automobile driven by the defendant collided with another, killing its driver. The defendant was taken to a hospital where she consented to a blood alcohol test to determine the percentage of alcohol in her blood. Four hours after the accident, a blood sample was taken by a hospital physician, who later testified that this was the first blood sample she had ever taken for the purpose of a blood alcohol test. She testified that the defendant's arm was wiped with a sponge containing either alcohol or tincture of Zephiran, an antiseptic alcohol, the syringe needle was inserted, and 30 cc. of blood was withdrawn and turned over to the police chemist for analysis. At the trial the defendant objected to the admission in evidence of the report of the analysis on the ground that the blood sample used was not a true indication of the percentage of alcohol in the defendant's blood. It was an erroneous indication, said the defendant, because alcohol was permitted to mix with the blood sample when the attending physician inserted and withdrew the syringe needle through the alcohol she had used to wipe the defendant's arm. As a result the alcohol percentage was increased upon analysis. This possibility was admitted by the police chemist, and an expert was called as a witness for the defendant. The expert added that the alcoholic content would be even more greatly increased if the physician placed the wet sponge over the needle as she withdrew it from the defendant's arm. A deputy district attorney then volunteered to submit to an experiment to test the percentage of probable error. Without objection from the defendant, blood was taken from both arms, one saturated with alcohol and the other dry, and the two samples were turned over to the police chemist for analysis. Subsequently the defendant objected to the chemist's testifying to the results of the experiment on the ground that there was no proper showing that the conditions when the test blood was withdrawn were the same as when the blood was withdrawn from the defendant. The objection was overruled, however, and the chemist testified that the arm saturated with alcohol yielded a blood alcohol percentage of 0.016, whereas the dry arm yielded a percentage of 0.006. This error if subtracted from the defendant's original blood percentage of 0.155 would leave 0.139, and, if four hours of oxidation of alcohol were added to reading (the time elapsed between the accident and the blood test), the reading would be 0.199% blood alcohol. In the opinion of the witness, a person with 0.199% blood alcohol would be under the influence of intoxicating liquors.

The district court of appeals, 2d district, division 3, California, sustained the verdict of the trial court. Experiments must be taken under substantially the same conditions as those existing at the time the alleged occurrence took place, said the court, but the conditions need not be identical. It is sufficient if the conditions are sufficiently identical to render the experiment reliable and free from uncertainty. If the conditions are otherwise, the results are inadmissible. The court further held that the objection concerning the results of the experiment on the ground that the conditions were not sufficiently identical were too general. The defendant should have specified exactly what conditions were not the same, since neither the court nor the prosecution would know what particular conditions to correct.

Having found no reversible error in the records, the court affirmed the judgment of conviction. *People v. Modell, 300 P. (2d) 204 (Calif., Aug., 1956).*

MEDICAL NEWS

CALIFORNIA

Dr. Gerbode Honored.—St. Bartholomew's Hospital Medical College in London has awarded to Dr. Frank L. A. Gerbode, San Francisco, associate professor of surgery, Stanford University School of Medicine, San Francisco, its highest honor—election as an Honorary Perpetual Student. Dr. Gerbode, the 16th person to be so honored since the hospital's founding in 1123 A.D., served as an associate in surgery at St. Bartholomew's Hospital in 1949. He was recently chosen first vice-president-elect of the American College of Surgeons and is a past-president of the San Francisco Heart Association.

Dr. Livingston Appointed Scientific Director.—Dr. Robert B. Livingston, associate professor of physiology and anatomy, University of California School of Medicine at Los Angeles, has been appointed scientific director of the combined basic research programs of the National Institute of Mental Health and the National Institute of Neurological Diseases and Blindness, Bethesda, Md. He succeeds Dr. Seymour S. Kety, who asked to be relieved as scientific director to devote full time to laboratory investigations on cerebral blood flow. Dr. Livingston joined the faculty of Yale University School of Medicine, New Haven, Conn., in 1946 as assistant professor of physiology. He was also executive assistant to Detlev W. Bronk, LL.D., president of the National Academy of Sciences–National Research Council. During his tenure at Yale, Dr. Livingston conducted studies in Sweden on the relation between the vestibular and ocular motor mechanisms in the brain stem. In recent years, he has been interested in the neurophysiological basis of behavior.

Cancer Chemotherapy Laboratory.—A cancer chemotherapy laboratory, which also serves as headquarters for the pharmacology department of Stanford University School of Medicine, has been established on the Palo Alto campus. Prof. Avram S. Goldstein, the head of the department, will direct the new campus research facility, which was built and equipped with the aid of $50,000 from the National Cancer Institute of the U. S. Public Health Service, and $10,000 from university funds. A radioisotope laboratory also has been set up in the new space with gifts totalling $6,700 from the ladies auxiliary of the California department of the Veterans of Foreign Wars. Under a committee headed by Dr. Sidney Raffel, chairman, medical microbiology department, the radioisotope equipment will serve all departments of the medical school. An additional grant of $68,000 from the National Cancer Institute is supporting research for the first year. The program is two-fold: (1) investigation into the development of resistance of cancer cells to anticancer drugs, and (2) a search for new and more potent anticancer drugs, being conducted by Prof. Arthur Furst, Ph.D.

Los Angeles County Community Health Week.—The thirteenth annual Community Health Week in Los Angeles County will be observed March 17-24 as an all-out effort by citizens of Los Angeles County and various separated areas throughout California to prevent disease and promote health. The Community Health Association of Los Angeles sponsors this effort and it is carried out in cooperation with public and parochial schools, health and welfare agencies, service clubs, PTA groups, and business, labor, religious, and civic organizations. The theme for the week is "Health Begins at Home." The schedule for the two Sundays will be Health Day in Churches; for Monday, it will be Health and Safety Day; for Tuesday, School Health Day; Wednesday, Community Health Day; Thursday, Home and District Health Day; Friday, Hospitals, Health Departments, Voluntary Agencies and Business and Industrial Health Day; Saturday, Health Day in the libraries and in congregations worshiping on that day. A highlight will be an all-day schedule on Wednesday at the Biltmore Hotel, wh e in the morning in "The Great Health Show" children and adults will participate in a dramatic portrayal of community health needs and resources. Along with the show will be exhibits and demonstrations and a panel presentation on mental health. After the show will be the Leadership Luncheon, at which Dr. Louis Bauer of New York, secretary general of the World Medical Association and a past-president of the American Medical Association, will speak on Building Health in Our World. Dr. C. M. Sellery, director, health service and health education in the Los Angeles city schools will speak on Health Begins at Home. In the afternoon at the Biltmore, a Round Table Health Exchange will be moderated by Dr. L. S. Goerke of the University of California at Los Angeles. The general chairman of Health Week is its founder, Dr. Ruth J. Temple, who now heads the office of special health services for the health department of the city of Los Angeles.

COLORADO

New Medical Research Center.—The Lasdon Foundation, a nonprofit organization with headquarters in Yonkers, N. Y., announces plans for a medical research center in Boulder, to be known as the Lasdon Foundation Research Institute of Chemotherapy. The center, which will be under the direction of Max N. Huffman, Ph.D., former head, organic chemistry section, Oklahoma Medical Research Foundation and professor of research biochemistry at the University of Oklahoma School of Medicine, Oklahoma City, will have facilities for research in medicinal chemistry and for pilot plant production for clinical studies. It will conduct research on cancer, atherosclerosis, arthritis, mental diseases, hypertension, viral and fungal dis-

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

eases, and the stimulation of the reticuloendothelial system. Dr. Huffman has served as professor of biochemistry at Southwestern Medical School of the University of Texas, Dallas.

CONNECTICUT

Dr. Haggard Resigns As Director.—Dr. Howard W. Haggard, founder of the Center of Alcohol Studies at Yale University, New Haven, has resigned as director of the Laboratory of Applied Physiology at the university. He will continue to serve as an advisor to the laboratory and to the center and as editor of the *Quarterly Journal of Alcohol Studies*, a post he has held since the journal was established in 1940. Dr. Haggard joined the Yale faculty in 1919. He was instrumental in organizing the Summer School of Alcohol Studies at Yale, now in its 14th year, and the Yale Plan Clinic. Colleagues estimate that during 30 years he personally raised more than 2 million dollars for the laboratory and its projects. Dr. Haggard is the author of "Devils, Drugs and Doctors," "The Lame, the Halt, and the Blind," "Staying Young Beyond Your Years," and "Alcohol Explored."

GEORGIA

Phi Delta Epsilon Lecture.—The Beta Nu chapter of Phi Delta Epsilon fraternity at the Emory University School of Medicine, Emory University, will hold its 11th annual lectureship March 13, 12:30 p. m., in the Grady Hospital Junior Lecture Room. The guest speaker will be Dr. Robert J. Huebner who will discuss "The Clinical Importance of the Adenoviruses."

ILLINOIS

Personal.—Dr. John D. Bealer, until recently in the U. S. Navy, has been named to the newly created post of medical director of the A. E. Staley Manufacturing Co., corn and soybean processing company, Decatur. Dr. Bealer served as intern at St. Luke's Hospital, Bethlehem, Pa., before entering the Navy.

Grant for Rabies Research.—A three-year grant of $30,000 annually has been made available for research on rabies in wildlife in Illinois, according to Dr. Harlow B. Mills, chief of the Illinois natural history survey. The grant comes from the National Institute of Health of the U. S. Department of Health, Education, and Welfare.

Chicago

Flexner Scholarship.—A $10,000 subsidiary scholarship in honor of Abraham Flexner, LL.D., New York, has been established at the Chicago Medical School by the Joshua B. and Esther F. Glasser Fund. The National Fund for Medical Education recently honored Dr. Flexner with a dinner in New York at which he was presented with the Frank H. Lahey memorial award for outstanding leadership in medical education.

Personal.—Dr. Lloyd J. Roth, assistant professor, department of pharmacology, University of Chicago, since 1952, has been named chairman of the department to succeed Dr. Eugene M. K. Geiling, Frank P. Hixon Distinguished Service Professor, who has retired after 20 years as head of the department. During the war Dr. Roth was a research officer in the U. S. Army in the chemical warfare service.

Hospital News.—Dr. Jack van Elk, native of Utrecht, Holland, has been named chief of the cardiovascular laboratory administered at Mercy Hospital by the Stritch School of Medicine of Loyola University. Dr. van Elk formerly was an attending physician to a hospital maintained by Standard Oil Co. for its employees on the Island of Aruba, off the coast of Venezuela. At the University of Colorado School of Medicine, Denver, he was in charge of the cardiovascular laboratory, working under Drs. Samuel G. Blount Jr. and Henry Swan II, Denver.

MASSACHUSETTS

Lecture by Dr. Dameshek.—The Alpha Omicron chapter of Phi Delta Epsilon fraternity at Boston University School of Medicine will hold its annual lectureship March 20. The guest speaker will be Dr. William Dameshek, professor of medicine, Tufts College Medical School, Boston, who will discuss "Polycythemia and Related States."

Annual Symposium at Naval Hospital.—The fifth annual Military Medico-Dental Symposium under the auspices of the commandant, first Naval district, will be held at the Naval Hospital, Chelsea, and civilian institutions in Boston, March 20-22. The program will provide information to reserve and regular medical department officers on current concepts in varied fields of the armed forces. The meeting on the first day will be at the Naval Hospital in Chelsea. On the morning of the second day a tour of the Harvard University School of Public Health, Boston, will be conducted by Dr. John C. Snyder, dean of the school. Lectures will be given at the Jimmy Fund Auditorium after the tour and also on the third morning; afternoon lectures will be given at this building and in the Joslin Auditorium at the New England Deaconess Hospital, Boston, and at the Naval Hospital, Chelsea. Among the speakers on the opening day will be Dr. Frank B. Berry, assistant secretary of defense for health and medicine; Rear Adm. Bartholomew W. Hogan, surgeon general of the Navy; Major Gen. Silas B. Hays, surgeon general of the Army; Dr. Howard F. Root, president, Massachusetts Medical Society; Capt. Shields Warren, professor of pathology, Harvard Medical School; Dr. Chester S. Keefer, director, Boston University School of Medicine; and Agnes Ohlson, R.N., president, American Nurses' Association. Capt. R. Cannon Eley, Naval reserve, assistant clinical professor of pediatrics, Harvard Medical School, is general chairman of the symposium, which has been approved for retirement point credit for the attendants on the active status list in the armed services reserve program.

MICHIGAN

Franklin Lectures in Detroit.—Wayne State University, Detroit, announces its seventh spring series of Leo M. Franklin Lectures in Human Relations to be presented at 5 p. m. on Sundays in the lecture hall of the Detroit Institute of Arts. Spring speakers and their topics include:

March 10, Edmond W. Sinnott, Ph.D., dean emeritus, school of graduate studies, Yale University, New Haven, Conn., The Questing Inheritance of Human Kind.
March 24, William Brown, director, Bureau of Educational Research, North Carolina College, The Human Potentials for Questing.
April 7, Ralph D. Rabinovitch, director, Hawthorne Children's Center in Michigan, Ann Arbor, The Hazards of Being Human.
April 28, F. Ashley Montagu, Ph.D., physiological anthropologist, Princeton, N. J., The Young of Human Kind.
May 12, Marie Rasey, professor of educational psychology, Why Teachers?

Clinical Institute.—The Michigan Clinical Institute will be held March 13-15 at the Sheraton-Cadillac Hotel, Detroit. The Wednesday session will close with a surgery panel moderated by Dr. Frederick A. Coller, Ann Arbor, for which the participants will be the speakers on the day's program: Drs. John H. Garlock, New York City; John H. Gibbon Jr., Philadelphia; L. Henry Garland, San Francisco; Charles B. Huggins, Chicago; Frank H. Mayfield, Cincinnati; Ralph C. Moore, Omaha, Neb.; and Charles L. Marsh, Valley, Neb. At 9 a. m. Thursday Dr. Howard B. Sprague, Brookline, Mass., will serve as moderator for a panel, "The Heart Patient at Work." Other out-of-state speakers on the Thursday program will be Drs. Donald E. Cassels, Chicago; William B. Kountz, St. Louis; and Julius Bauer, Los Angeles. The sessions will close Friday afternoon with "Diabetic Legs" by Dr. Frederick W. Williams, New York City, and "Arthritis in Patients Over Sixty" by Dr. L. Maxwell Lockie, Buffalo.

NEW JERSEY

Society News.—The recently organized New Jersey Society of Internal Medicine has selected a provisional steering committee consisting of Drs. Frederick Hnat, Elizabeth; Sherwood Vine, Trenton (provisional chairman); Leslie M. Townsend, Roselle Park; and Peter J. Warter, Trenton. Internists in New Jersey may obtain information by writing to Dr. Sherwood Vine, 208 W. State St., Trenton.

Meeting on Heart Disease.—The eighth annual Professional Education Seminar on Heart Disease will be presented by the New Jersey Heart Association March 20 (afternoon) at the Hotel Essex House, Newark, under the chairmanship of Dr. John A. Kinczel, Trenton. A panel discussion, "Problems of Hypertensive Disease" will precede the presentation of two cases for a clinicopathological conference by the panel members. All physicians in the state are invited to attend. The moderator will be Dr. Robert W. Wilkins, Boston; the pathologist, Dr. William E. Ehrich, Philadelphia; and the panel members, Drs. Arthur M. Fishberg and George A. Perera, New York City, Edward D. Freis, Washington, D. C., and William A. Jeffers, Philadelphia.

Personal.—Dr. Henry A. Davidson, Cedar Grove, assistant superintendent of the Essex County Overbrook Hospital, conducted a two-day seminar at the Veterans Administration Hospital, Jefferson Barracks, Mo. The subjects of his lectures were: "Appraisal of Competency in a VA Hospital," "Criminal Responsibility," and "Doctor as a Witness."——Dr. Charles I. Silk, Perth Amboy, president, New Jersey Trudeau Society, was honored at the annual spring conference of the New Jersey Tuberculosis and Health Association and the New Jersey Trudeau Society. In presenting a certificate of merit, Dr. Harry J. White of Metuchen, president of the New Jersey Tuberculosis Association, cited Dr. Silk's many years of public-spirited service and outstanding leadership in the prevention and control of tuberculosis in New Jersey.

NEW YORK

Psychiatric Center in Brooklyn.—The second day hospital to be organized by the New York State Department of Mental Hygiene was recently opened at 105 Schermerhorn St., Brooklyn. The center occupies the fourth and fifth floors at this address, where the Brooklyn aftercare clinic is located. It is designed for the care of 40 to 50 adults, 18 years or older, and will operate five days a week from 9:30 a. m. to 4:30 p. m. The treatment program consists of individual and group psychotherapy, social casework, drug and electric shock therapy, occupational and recreational therapy, and a sheltered workshop stressing development of job readiness. Dr. Donald M. Carmichael is director of the aftercare clinics, and Dr. Elizabeth Huff is psychiatrist in charge.

Dr. Lawrence Kohn Honored.—Dr. Lawrence A. Kohn, associate professor of medicine at the University of Rochester School of Medicine and Dentistry, was recently given the gold medal of that school's medical alumni association. Dr. Kohn, who has been associated with the Medical Center of the University of Rochester for 30 years, was the first chief resident physician appointed to the Strong Memorial Hospital staff in 1926. In presenting the medal, Dr. Matthew E. Fairbank, retiring president of the association, said in part: "All alumni recognize him as a great teacher and clinician who has lit many fires of enthusiasm among young men in medicine. The alumni of the School of Medicine and Dentistry can think of no better way of expressing their gratitude, affection and esteem than by bestowing on him their gold medal, their highest award."

Postdoctoral Fellowships at Rochester.—In fulfillment of a bequest from the estate of the late Ralph Hochstetter of Buffalo, four groups of postdoctoral research fellowships to be awarded to graduates of approved medical schools have been established at the University of Rochester School of Medicine and Dentistry,

according to Dr. Donald G. Anderson, dean of the school. Under terms of the will, oil and gasoline royalties and other securities were divided equally between this medical school and the University of Buffalo Medical School. The University of Rochester fellowships, to be named the Bertha H. Buswell and Dr. Henry C. Buswell fellowships in memory of Mr. Hochstetter's late sister and her late husband, permit recipients to pursue research in any of the departments of the medical school. They include:

1. Junior fellowships for promising young graduates who have completed one year of internship and preferably their residency and who wish to prepare for careers in medical research. These may be renewed for a second or third year.

2. Senior fellowships for young medical graduates desiring to continue careers in medical research, who have completed their hospital training and who have had one or two years of fellowship training as Buswell junior fellows or who have had comparable experience in medical research. The senior fellowships may be renewed for a total of five years.

3. Faculty fellowships, to be awarded to assistant professors (or higher) who are graduates of approved medical schools and who have established themselves as independent medical investigators and continue to be actively engaged in research. The faculty fellowships will be for an indefinite period.

4. Distinguished service fellowships, to be awarded to associate professors or full professors on the medical school faculty engaged in medical research who have made outstanding contributions to medical science. These fellowships will be for an indefinite period.

New York City

Bela Schick Lecture.—The 14th Bela Schick Lecture, "A Quarter of a Century with Prematures," will be delivered by Dr. Sam Z. Levine, pediatrician-in-chief and professor of pediatrics, The New York Hospital–Cornell Medical Center, March 11, 8:30 p. m., in the Blumenthal Auditorium.

Annual Safety Convention.—An estimated 8,000 safety experts and accident prevention workers will convene at the Hotel Statler March 18-22 for the 27th annual Safety Convention and Exposition under sponsorship of the Greater New York Safety Council and with the cooperation of 70 agencies including the Army, Navy, Atomic Energy Commission, Red Cross, branches of city and state governments, and business, civic, and engineering organizations. In conjunction with the convention, the safety council will hold an exposition of developments in safety devices, protective equipment, demonstrations of psychophysical tests, and other aids to accident prevention.

NORTH CAROLINA

Society News.—The new officers of the North Carolina Pediatric Society are Drs. Charles F. Williams, Raleigh, president; George Watson, Durham, vice-president; and Bailey Webb, Durham, secretary-treasurer.

Personal.—Dr. Harold D. Green, director, department of physiology and pharmacology, Bowman Gray School of Medicine, Wake Forest College, Winston-Salem, delivered the 40th Mellon Lecture before the Society for Biological Research of the University of Pittsburgh School of Medicine, Nov. 6, 1956 on "Autonomic Control of the Circulation in the Major Vascular Beds."——Dr. Sidney S. Chipman, clinical professor of pediatrics, University of North Carolina School of Medicine, Chapel Hill, recently took a month's trip to the Philippines and Japan as an advisor to personnel in the Far East Air Force who have their families with them. Last year Dr. Chipman had a similar appointment in Europe with the Air Force. In 1953 he was in Japan and the Far East as a maternal and child health consultant for the World Health Organization of the United Nations.

Grants in Psychiatry.—Dr. George C. Ham, chairman, department of psychiatry, University of North Carolina School of Medicine, Chapel Hill, has announced receipt of about $150,000 in grants from the National Institute of Mental Health of the U. S. Public Health Service for the present fiscal year. These grants include funds for (1) stipends for residents in psychiatry and salaries for staff members to supplement the regular department staff's instruction in this specialty; (2) a pilot project to explore the possibility of more effectively teaching and integrating basic psychiatric concepts with the other basic medical science disciplines; (3) an experimental teaching plan for first-year medical students oriented toward the multidisciplinary study of human illness; (4) development of a program of training, research, and service in child psychiatry; and (5) extension and expansion of a psychological internship program in the department of psychiatry. With the exception of the grant for child psychiatry, these grants represent continuing programs begun from one to three years ago. The child psychiatry unit was only recently organized under the guidance of Dr. Lucie N. Jessner, professor of psychiatry.

OHIO

Dr. Vilter Succeeds Dr. Blankenhorn.—Dr. Richard W. Vilter, who has been affiliated with Cincinnati College of Medicine since 1938, has been appointed director of the department of internal medicine, succeeding Dr. Marion A. Blankenhorn, who retired Sept. 1 with the status of professor emeritus. For the United Nations World Health Organization, Dr. Vilter has filled assignments in Egypt, Guatemala, and Panama, studying ways of overcoming prevalent nutritional deficiencies. He has also held consultant and other appointive posts with the office of the surgeon general and the National Research Council.

Personal.—Dr. Norton H. Bare, chief of the staff at the Apple Creek State Hospital, has been appointed assistant superintendent of the Training School at St. Marys, W. Va.——Dr. George James, formerly director of health of the city of Akron, has been named deputy commissioner of the New York City Department of Health. Dr. James was assistant commissioner of the New York State Department of Health from 1952 to 1955.——Dr. Robert M. Stecher, Cleveland, recently returned from a three months' tour of Europe and Africa, during which he addressed the International Congress of Human Genetics in Copenhagen, Denmark. A paper on "The Nature of Osteoarthritis" was

presented at the Scandinavian Rheumatism Congress in Lund; the Pretoria Medical School in Pretoria, Union of South Africa; the Witwatersrand University Medical School in Johannesburg; and the Cape Town University Medical School in Cape Town. During his stay in Africa he discussed "The Nature of Gout" before the medical society in Port Elizabeth and "The Heredity of Rheumatic Fever" before the Natal Medical School in Durban.

OKLAHOMA

Society News.—The January issue of the *Bulletin of the Tulsa County Medical Society* is dedicated to the golden anniversary of that organization.

Personal.—Dr. John W. Phillips, was recently honored by a community testimonial observance in the high school auditorium of his home town, Oilton, which he served as mayor for 10 years. Dr. Phillips has retired from the practice of surgery at Cushing Municipal Hospital after 35 years.——Dr. Herbert Kent, associate professor, department of physical medicine, Oklahoma University Medical Center, Oklahoma City, spoke to the Indiana planning committee on rehabilitation at Indianapolis, Nov. 9, on "Physical Medicine and Rehabilitation in Oklahoma."

Dr. Dolan Honored.—The Gladys K. Dolan, M.D., Fund has been created to provide needy children at the Children's Medical Center in Tulsa with appliances, shoes, and orthopedic equipment. The fund was established by the center's auxiliary in recognition of Dr. Dolan's contributions to the health and welfare of young patients. A staff member of Children's Medical Center since 1954, Dr. Dolan is a full-time worker. However, only a portion of her work is salaried, and she contributes the rest of her time. She was formerly a staff member of the Tulsa City-County Health Department.

VERMONT

Medicolegal Meeting.—The Vermont Association for Mental Health will sponsor a meeting on "Law and Psychiatry" for the Vermont State Medical Society and the Bar Association March 14 in Burlington where Dr. Gregory Zilboorg, New York City, will speak. A panel of three lawyers and three physicians will discuss the right or wrong test and the Durham decision.

WASHINGTON

Society News.—The new officers of the Walla Walla Valley Medical Society include Dr. Clifford D. Hogenson, president; Dr. Robert A. Campbell, vice-president; and Dr. Robert W. Jamison, secretary-treasurer, all of Walla Walla.

Defense Award to Tacoma Hospital.—Tacoma General Hospital, Tacoma, is the first medical activity to receive the Department of Defense reserve award established by Secretary of Defense Wilson in 1955. The hospital sponsors the Army 359th General Medical Reserve Unit. Criteria used in the selection of recipients are the policies practiced toward reservist programs. These policies include leave in addition to annual leave for the reserve tours required of the reservists; emergency duty with full pay or the difference between military and company pay; hiring, promotion, or transfer of reservists without discrimination; and assistance to reservists in making scheduled inactive duty drills and tours of active duty for training purposes. The Tacoma General Hospital provides a separate building of eight rooms for use of the reserve unit it sponsors and has made available the hospital auditorium, motion picture equipment, training aids, and supplies of various kinds.

GENERAL

Symposium on the Reticular Formation of the Brain.—At an international symposium held March 14-16 under the auspices of the Henry Ford Hospital, Detroit, the contributors will be members from neuroanatomic and neurophysiological groups from England, France, Italy, Sweden, Australia, the United States, and Canada. Attendance is by invitation. Anyone interested who has not received an invitation may write to Dr. William C. Noshay, Henry Ford Hospital, Detroit 2.

Fellowship in Dermatology.—A resident fellowship in the department of dermatology, Northwestern University Medical School, Chicago, has been established by the Gillette Company. The fellowship carries an award of $2,000 a year for an unmarried student and $2,500 for a married student. An additional fund of $1,500 will be provided for the expense of training the resident. The grant is annual and will be known as the Gillette-Toni fellowship in dermatology. The recipient will be named in 1957 by Dr. Herbert Rattner, Chicago, chairman of the department.

Blood Bank Awards.—At a banquet Sept. 4, 1956, the American Association of Blood Banks presented Karl Landsteiner awards to Dr. Philip Levine, Raritan, N. J., and Dr. Alexander S. Wiener, Brooklyn, N. Y. The award is given annually to the person who has made the most outstanding contribution to the field of blood banking. For the first time this year the association also gave the John Elliott award, which is to be made each year to a member of the association for an outstanding piece of original investigation. The recipient was Dr. J. Garrott Allen, Chicago.

Fellowships for Residents in Ophthalmology.—Six additional fellowships for residents in ophthalmology, to begin July 1, have been announced by the Guild of Prescription Opticians of America. Each fellowship is for a total of $1,800, payable in monthly stipends over the period of a three-year residency. The grants are limited to residencies at approved institutions where full three-year residencies are offered. Information is available at the Guild of Prescription Opticians of America, 110 E. 23rd St., New York 10. Applications must be received by May 15.

Society Changes Date.—The Society of Medical Group Psychoanalysts, which was to have met March 6 (THE JOURNAL, Feb. 23, page 665), will hold its first scientific meeting at the New York Academy of Sciences, 2 E. 63rd St., New York City, March 22, 8:30 p. m. Dr. Louis Landman, New York City, will moderate a discussion on "Group Psychoanalysis Today" by Drs. Nathan W. Ackerman, Sidney Rose, and Alexander Wolf, all of New York City. The society is presently open for charter membership. Those interested should write to Dr. Benjamin Wassell, Acting Secretary, 49 E. 78th St., New York 21.

Bequests to Medical Foundation.—Southwestern Medical Foundation was recently named beneficiary of two estates in Dallas, Texas. The Fred and Louise McClurkin bequest, valued in excess of $100,000 in stocks and cash from the estate of Louise McClurkin, will be used in Dallas in the aid of science for the prevention and cure of poliomyelitis and diseases of the heart. Under terms of the will of Mrs. Edith Eulalie Sewell Lee, her estate of about $250,000 will go to the foundation after the death of the last of four relatives, who will receive the income from the estate during their lifetimes.

Medical Tours After A. M. A. New York Meeting.—The following special tours to Europe and Bermuda have been planned to follow the A. M. A. Annual Meeting in New York, June 3-7: (1) a 24-day tour to France, Italy, Switzerland, Belgium, and England; (2) a 38-day tour to these countries and also to the Netherlands and Germany; and (3) tours to Bermuda, which will be offered either by air or in an air-and-sea combination. All the tours, especially planned for the interest of physicians, include medical meetings in major cities. Information may be obtained from Lee Kirkland Travel, 1231 Baltimore, Kansas City, Mo., or Medical Tours, P. O. Box 3433, Chicago 54.

Simmons Memorial Professorship Fund.—Friends of the late Brig. Gen. James S. Simmons, M.D., have given $150,000 toward an endowed professorship in his name at the Harvard School of Public Health, Boston. The committee of sponsors, of which Dr. George C. Shattuck is chairman, invites other friends and colleagues to contribute in order that the professorship may be activated as soon as possible. Gifts to date are sufficient to guarantee the permanence of the professorship. When accumulated income on the endowment and additional gifts have brought the fund to $400,000, a James Stevens Simmons Professor will be appointed. Checks should be made payable to Harvard University.

Basic Science Certificates Lost.—The Minnesota State Board of Examiners in the Basic Sciences reports that two basic science certificates issued during 1956 have disappeared. These certificates were made out as follows:

Hugh Joseph Hughes, Jr., dated October 3, 1956, issued on the basis of examination before our Board.

Milton Henry Seifert, Jr., dated January 4, 1956, issued on the basis of examination before our Board.

Examining boards are notified that these certificates have been rendered null and void. Should they appear, please return them to Raymond N. Bieter, Secretary-Treasurer, Minnesota State Board of Examiners in the Basic Sciences, Minneapolis.

Competition for Blakeslee Awards.—The American Heart Association announces that the 1957 competition for Howard W. Blakeslee awards for reporting in the field of heart and blood vessel diseases will close May 1. Entry blanks may be obtained from the association, 44 E. 23rd St., New York 10. Winning work will be selected from among newspaper and magazine articles, books, radio and television programs, and films published or produced between March 1, 1956, and Feb. 28, 1957. The awards carry an honorarium of $500 each. The awards were established in 1952 as a memorial to the late Howard W. Blakeslee, science editor of the Associated Press and founder of the National Association of Science Writers, who died of heart disease.

Oak Ridge Offers Computer Service.—The Oak Ridge (Tenn.) Institute of Nuclear Studies will make available to universities throughout the region the services of the Oak Ridge automatic computer and logical engine. The program will assist university research programs by speeding some computations and making feasible others that time and cost have hitherto made prohibitive. Theodore W. Hildebrandt, Ph.D., director of the program, will travel to university campuses on request for discussions of problems suitable for computation with this machine. Each university will be charged a moderate fee for time and travel needed for work on its problems. Information may be obtained by writing Dr. Hildebrandt, P. O. Box 117, Oak Ridge, Tenn.

Grants in Muscular Dystrophy.—The National Muscular Dystrophy Research Foundation (709 Main St., Liberty, Texas) has made grants for (1) a second-year renewal of the project of Dr. Harold L. Dobson, assistant professor of medicine, Baylor University College of Medicine in Texas Medical Center, Houston; (2) the first year's work by Walter B. Geiger, Ph.D., a senior research associate of the Southwest Foundation for Research and Education in San Antonio on his study, "Enzymological Transformations of Creatine in Muscle"; and (3) Roy B. Mefferd, Jr., Ph.D., for his project, "Excretion Patterns of Families with Muscular Dystrophic or Spinal Muscular Atrophic Members . . ." at the University of Texas Biochemical Institute at Austin, made possible from a donation by the Muscular Dystrophy chapter of San Antonio.

Grants in Cardiology.—The American Heart Association and its affiliates recently awarded grants-in-aid totaling $1,042,817.36 to 180 scientists engaged in research in cardiovascular diseases. The new grants raise to about $1,873,000 the sums allocated by the heart association to support scientific research during the

fiscal year ending June 30, 1957. These are additional to 131 fellowships totaling $830,000 announced in 1956. According to Dr. Irvine H. Page, Cleveland, president, the association has channeled more than $15,250,000 into support of scientific research since it became a national voluntary health agency in 1948. These funds come from contributions by the public to the heart fund campaign conducted each February. Affiliated heart associations also appropriate a large share of their income to support scientific investigations in their own areas.

Grants in Problems of Sex.—The division of medical sciences of the National Academy of Sciences–National Research Council is accepting applications for grants-in-aid of research in problems of sex. The committee is concerned primarily with encouraging research on the mechanisms controlling sexual behavior in animals and man. Proposals involving endocrinological, neurological, psychological, anthropological, phylogenetic, and genetic studies directed toward this objective are invited. Requests will be considered that deal with the physiology of reproduction or with related biological and biochemical fields. Preliminary inquiries should be addressed to Room 309, Division of Medical Sciences, National Academy of Sciences–National Research Council, 2101 Constitution Ave. N. W., Washington 25, D. C. Completed applications for the fiscal year 1957-1958 should be postmarked on or before April 1.

Cancer Cytology Congress.—The First Pan American Cancer Cytology Congress will be held at the Eden Roc Hotel, Miami Beach, Fla., April 25-29. The congress is supported by a grant from the Department of Health, Education, and Welfare of the U. S. Public Health Service, and the U. S. Department of State has mailed invitations to the health ministries of 21 nations of the Pan-American area. The congress, whose theme will be "Cancer Protection Through Early Detection," is sponsored by the Southern Society of Cancer Cytology; the Cancer Cytology Foundation of America, New York; the University of Miami; and the Cancer Institute at Miami. Inquiries may be addressed to Dr. Wayne S. Rogers, program chairman, Dr. Homer L. Pearson Jr., chairman scientific exhibits, Dr. Joseph H. Rudnick, chairman of commercial exhibits, Dr. George O. Gey, Johns Hopkins University, Baltimore, secretary of the congress, or to Dr. James E. Ayre, general chairman, P. O. Box 633, Coral Gables, Fla. Early reservations are advised.

Society News.—At the annual meeting in St. Louis, Oct. 11, the **American Board of Dermatology** elected Dr. John H. Lamb, Oklahoma City, president; Dr. J. Lamar Callaway, Durham, N. C., vice-president; Dr. Beatrice M. Kesten, New York, secretary-treasurer (reelected); and Dr. Walter C. Lobita Jr., Hanover, N. H., assistant secretary. The office of the board is at 1 Haven Ave., New York 32.——Officers of the **Radiological Society of North America** include president-elect, Dr. Sydney J. Hawley, Seattle; president, Dr. C. Edgar Virden, Kansas City, Mo.; vice-presidents, Drs. Richard H. Chamberlain, Philadelphia, Maurice D. Frazer, Lincoln, Neb., and Harold P. Tompkins, Los Angeles; and secretary-treasurer, Dr. Donald S. Childs, Syracuse, N. Y.——The **Association of Medical Illustrators** recently elected the following officers: president, Mr. Lee Allen, department of ophthalmology, State University of Iowa College of Medicine, Iowa City; vice-president, Miss Gladys McHugh, University of Chicago clinics; recording secretary, Miss Patricia O'Neill, Southwestern Medical School of the University of Texas, Dallas; corresponding secretary, Miss Rose M. Reynolds, University of Nebraska College of Medicine, Omaha; and treasurer, Mr. Melford Diedrick, University of Buffalo School of Medicine.

Fellowships in Allergy.—The American Foundation for Allergic Diseases, 274 Madison Ave., New York 16, announces three fellowships in research and clinical allergy for two years each, carrying a stipend of $4,500 for the first year, $4,750 for the second, and a total of $750 for laboratory and travel expenses during the two-year period. The funds for these fellowships have been made available by Mr. John D. Rockefeller Jr., in a grant to the foundation.

Unlike the usual procedure, the foundation has established single fellowships with three investigators qualified to teach in this field and in institutions where adequate clinical facilities exist. Applicants should apply directly to one of the following investigators, who will make the final selection: Dr. Frederick G. Germuth Jr., Associate Professor of Pathology, Johns Hopkins University Medical School, Baltimore 5; Dr. Colin M. MacLeod, Professor of Research Medicine, University of Pennsylvania, 820 Maloney Clinic, 36th and Spruce Streets, Philadelphia 4; or Dr. Herman N. Eisen, Professor of Medicine (Dermatology), Washington University School of Medicine, Saint Louis.

Candidates, who must have completed the graduate training required as a preliminary to certification by the boards of internal medicine or pediatrics, are to divide their time between research and clinical training, and in the second year 10 or 15% of a candidate's time might be devoted to teaching. Applications should be received by May 10, 1957.

Practitioners Meet in St. Louis.—The ninth annual scientific assembly of the American Academy of General Practitioners will convene at the Kiel Auditorium in St. Louis March 25-28, under the presidency of Dr. John S. DeTar, Milan, Mich. The sessions will open Monday afternoon with a panel, "Impact of Maternal Mortality Studies on Today's Obstetrics," for which Dr. Ralph A. Reis, Chicago, will serve as moderator and Drs. Harold S. Morgan, Lincoln, Neb., and Willis E. Brown, Little Rock, Ark., as collaborators. Tuesday afternoon a panel on recent advances in surgery will be presented by Dr. Clarence V. Kusz, Minneapolis (Vascular Surgery); Dr. Donald B. Effler, Cleveland (Thoracic Surgery); and Dr. John E. Webster, Detroit (Neurosurgery). At 4 p. m. Dr. I. S. Ravdin, Philadelphia, will moderate a panel on "Pre- and Post-Operative Care," with Drs. John Adriani,

New Orleans, and Joseph W. Telford, San Diego, Calif., as participants. A symposium on therapy is scheduled for Wednesday, 1:30 p. m. Dr. H. Mitchell Perry, St. Louis, will discuss "Hypertension"; Dr. Frank M. Berger, New York City, "The Tranquilizers"; and Dr. Edward H. Rynearson, Rochester, Minn., "Use and Abuse of Hormones." The sessions will close at 11:30 a. m. Thursday with a lecture on "Internal Obstruction" by Dr. Philip Thorek, Chicago. On Wednesday at 8 p. m. Dr. Malcome Phelps, El Reno, Okla., will be installed as president of the academy. An invitational scientific congress is scheduled in New Orleans for March 29, following the assembly. The program will be sponsored by the Louisiana Academy of General Practitioners.

FOREIGN

Meetings on Endocrinology.—The Society for Endocrinology will hold its 60th meeting (March 20 at 1 Wimpole St., London W. 1) as a joint symposium with the section of endocrinology, Royal Society of Medicine. The subject will be "Investigations on Subjects Relating to Obesity and Diabetes." The annual general meeting of the Society for Endocrinology will be held May 3 at the Zoological Society of London. The annual lecture will be given by Prof. C. de Duve of Louvain, at Manson Hall, Portland Place, May 8, on "The Present Status of Glucagon."

Seminar Congresses in Surgery.—In seminar congresses in surgery the American Medical Society of Vienna will present the following programs by the medical faculty of the University of Vienna:

April 3-5, Surgical Errors and Safeguards.
May 2-4, Thoracic Surgery.
June 4-6, Gastrointestinal Surgery.
July 2-4, Cardiovascular Surgery.
Aug. 6-8, Neurosurgery.
Sept. 3-5, Urological Surgery.
Oct. 1-3, Surgical Treatment of Liver, Gallbladder.
Nov. 5-7, Plastic and Oral Surgery.

The program for the seminar congress in orthopedic and traumatic surgery includes:

April 19-20, Imperative Traumatic Surgery.
May 17-18, Treatment of Congenital Orthopedic Deformation.
June 21-22, Fractures of the Extremities.
July 19-20, Rehabilitation.
Aug. 23-24, Surgical Treatment of Joints.
Sept. 20-21, Intramedullary Nailing.
Oct. 18-19, Cranial and Spinal Injuries.
Nov. 22-23, Surgical Treatment of the Hand.

Details may be obtained from the American Medical Society of Vienna, Universitatsstrasse 11, Vienna I. Cable: "Ammedic," Vienna.

CORRECTION

Dr. Frank H. Mayfield.—In the footnote to his article in THE JOURNAL, Jan. 26, 1957, page 245, Dr. Mayfield was said to be Professor of Neurosurgery, University of Cincinnati College of Medicine. This statement was erroneous. Dr. Mayfield was Assistant Professor of Clinical Surgery, but resigned in 1951 to accept appointment to the Board of Directors of the University of Cincinnati.

EXAMINATIONS AND LICENSURE

AMERICAN BOARD OF ANESTHESIOLOGY: *Part I.* Various locations, July 19. Final date for filing application was Jan. 19. *Oral.* Asheville, No. Car., Mar. 24-29. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written.* Several cities, June 27. *Oral.* Baltimore, Oct. 11-13. Final date for filing application is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 21. *Oral.* Boston, April 3-6. Final date for filing application was Jan. 2. Chicago, May 27-29; San Francisco or Los Angeles, September. Final date for filing application was Feb. 1. *Subspecialties. Gastroenterology.* Philadelphia, April 5-6. Final date for filing application is March 1. Exec. Sec., Dr. W. A. Werrell, 1 West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part II.* Chicago, May 15-25. Final date for filing application was Feb. 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* New York, May 23-27; Chicago, Oct. 7-11. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland 9, Maine.

AMERICAN BOARD OF OTOLARYNGOLOGY: Chicago, Oct. 7-11. Final date for filing application is April. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I.* Washington, D. C., Los Angeles and St. Louis, Mo., April 18. *Part II.* New York City, Jan. 29-31, 1958. Final date for filing application is August 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF PATHOLOGY: *Oral and Written. Pathologic Anatomy and Clinical Pathology.* Washington, April 4-6. Final date for filing application is March 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, Indianapolis 7.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Parts I and II.* New York City, June 8-9. Final date for filing application is March 1. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY: *Entire Examination.* Philadelphia, May 4-6. Final date for filing case reports was Jan. 1. Corres. Sec., Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Oral and Written. Public Health.* Schools of Public Health, April 11-13. *Aviation Medicine.* Denver, May 9-11. *Occupational Medicine.* St. Louis, April 26-28. Sec., Dr. Thomas F. Whayne, 615 North Wolfe St., Baltimore.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written. Parts I and II.* September. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New Orleans, Mar. 18-19. Final date for filing application was Sept. 10. New York, Dec. 16-17. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: Tampa, April 1-6. Final date for filing application was Jan. 1. Washington, Sept. 23-28. Final date for filing application is June 1. Within the near future a special examination for certification in Nuclear Medicine will be offered to diplomates in Radiology and Therapeutic Radiology. Application must be made before Feb. 15. Sec., Dr. B. R. Kirklin, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Part II.* Nashville, Mar. 11-12; Boston, April 8-9, and New York, June 10-11. Sec., Dr. John B. Flick, 225 S. 15th St., Philadelphia 2.

AMERICAN BOARD OF UROLOGY: February 1957. Sec., Dr. William Niles Wishard, 1711 N. Capital Ave., Indianapolis 7.

GOVERNMENT SERVICES

ARMY

Deadline for Training in Nuclear Medicine.—Army medical officers with a background in physical sciences and mathematics who are interested in becoming officers in nuclear medicine should apply by April 1, 1957, for admission to the nine-month formalized training course beginning about July 1, sponsored by the armed forces special weapons project. Announcement of limited space for this training was made by Col. Clinton S. Maupin, special assistant to the surgeon general for nuclear energy.

Assignments after completion of the course will be in the established Army career patterns for officers in nuclear medicine, including duty tours in biological research, clinical isotope usage, industrial radiology, and health physics and staff assignments in the field of nuclear medicine.

The course begins with five months of instruction at Reed College, Portland, Ore., followed by short courses at Hanford Atomic Works, Richland, Wash.; Sandia Base, N. Mex.; and Walter Reed Army Institute of Research, Washington, D. C. Applications should be submitted to the Surgeon General, Department of the Army, Washington 25, D. C., Attention: MEDCM-CG.

VETERANS ADMINISTRATION

Fellowships Available.—The Veterans Administration Hospital at 42nd Avenue and Clement Street, San Francisco, announces the availability of a fellowship in cardiology July 1. The one-year fellowship (stipend $300 a month) is supported by the San Mateo County Heart Association, the fellow being appointed from Stanford University School of Medicine. Appointments are renewable. Applicants must be graduates of class-A medical schools and citizens of the United States. Several fellowships (stipend beginning at $300 a month) are also available in hematology and chemotherapy of tumor and lymphoma, in conjunction with Stanford University School of Medicine. Fellowships are supported by the National Institutes of Health in conjunction with a research project.

Personal.—Dr. Paul L. Eisele, manager, VA Hospital, Waukesha, Wis., has been appointed manager of the VA Hospital in Albuquerque, N. Mex., succeeding David K. Dalager, who retired Feb. 28. The Albuquerque hospital is a 500-bed general medical and surgical facility.

Hospital News.—Dr. Earl C. Gluckman, director of professional services at the VA Hospital in the Bronx, N. Y., has been appointed manager of the VA Hospital at Coral Gables, Fla., to succeed Dr. Harold F. Machlan, who retired at Coral Gables Feb. 28.

PUBLIC HEALTH SERVICE

Examination for Public Health Educators.—A competitive examination for appointment of health educators as regular corps officers in the U. S. Public Health Service will be held throughout the country May 7-10. Application forms may be obtained from the surgeon general. Transcripts covering all undergraduate and graduate education should accompany application forms. Applications must be received by the Surgeon General, U. S. Public Health Service, Washington 25, D. C., no later than March 29.

Appointments are made in grades equivalent to the Navy grades of lieutenant junior grade and lieutenant. In the Public Health Service, these grades are categorized as assistant sanitarian (health educator) and senior assistant sanitarian (health educator). Notification of the results of examinations may be expected within about 45 days after the examinations. Applicants who are not interested in regular corps appointments are invited to apply for appointment in the reserve corps.

Candidates must be U. S. citizens and at least 21 years of age; they must have a master's degree from an accredited school of public health. Candidates for assistant sanitarian must have had at least seven years of collegiate and professional training and appropriate experience as a health educator. Candidates for senior assistant sanitarian must have had a total of 10 years of collegiate and professional training and appropriate experience.

The examination will include an oral interview and physical and written examinations, the latter including the following subjects: general environmental sanitation, hygiene, public health sciences and practices, community organization and principles, health education methods and materials, and administration of health education. Candidates who have a physical defect or who have had a serious illness or injury should attach a statement to the application, outlining in detail the nature of such illness or injuries, treatment received, periods of hospitalization, length of absence from work, and present status.

Health educators work at the local, state, interstate, national, or international level. They assist in the planning, development, and evaluation of health education programs. They are also engaged in exploratory and demonstration projects related to the application of health education principles and techniques in the various Public Health Service programs.

Entrance pay for an assistant sanitarian (health educator) with dependents is $4,817 a year. For a senior assistant sanitarian (health educator) with dependents, it is $5,718. These figures include subsistence and rental allowance. Appointments are permanent in nature, and promotions are made at regular intervals up to the equivalent to the Navy grade of lieutenant commander. Promotions to the grades of senior sanitarian and sanitarian director (health educator), which are equivalent to Navy commander and captain, respectively, are made by selection.

Retirement pay after 30 years of service or at age 64 is three-fourths of annual basic pay at the time of retirement. Active duty as a commissioned officer in the Public Health Service fulfills the obligations of selective service.

Training Available in Emergency Health Service.—Training in emergency health service is available to professional medical and health personnel, Dr. Leroy

E. Burney, surgeon general of the Public Health Service, announced Feb. 8. The training covers a wide variety of activities, including public health activities in national emergencies, epidemiology, advanced training for sanitary engineers, public health nursing, operation of emergency water supply equipment, radiologic monitoring, detection and control of radioactive pollutants in water, organization of communicable disease control programs, and active duty under actual emergency conditions. Confined principally to officers in the commissioned reserve of the Public Health Service, the training is made available either by attendance on active duty or through correspondence courses.

Between March, 1955, and June 30, 1957, over 500 commissioned reserve officers will have attended such courses in Public Health Service installations throughout the country. To date, courses have been held or are scheduled in Atlanta, Ga.; Cincinnati; Washington, D. C.; and San Francisco. Others are given by the Federal Civil Defense Administration, in Battle Creek, Mich.; by the Industrial College of the Armed Forces in Washington, D. C.; or in association with local health agencies throughout the country. A limited number of officers are training in Pittsburgh, Boston, Philadelphia, Oak Ridge (Tenn.), and San Antonio (Texas). Courses are being developed for other locations.

The commissioned reserve is open to physicians, nurses, dentists, sanitary engineers, pharmacists, veterinarians, psychologists, bacteriologists, microbiologists, medical record librarians, statisticians, health educators, medical and psychiatric social service workers, and other professional personnel actively engaged in preventive medicine and public health practice. Applicants must meet the requirements for appointment but need not have had experience in the public health field to be eligible. No officer of the commissioned reserve will be called to active duty without his consent, unless a national emergency has been declared.

World Health Day.—The United States is joining with other nations in observing world health day, April 7, Dr. Leroy E. Burney, surgeon general of the Public Health Service, announces. Federal agencies will observe the theme "Food and Health" in programs dealing with nutrition, food production and distribution, and food protection and sanitation. Agencies participating include the Department of Health, Education, and Welfare; the Department of Agriculture; and the Department of State.

In cooperation with the national citizens committee for the World Health Organization, the government committee for World Health Day will also meet requests for material from industries and voluntary groups that plan to observe the day. Special kits of material will be prepared for this purpose. Dr. H. van Zile Hyde, chief, Public Health Service division of international health, is chairman of the interagency committee.

The World Health Day theme was selected by the World Health Organization to commemorate the anniversary of the adoption of the constitution of the World Health Organization. A different theme is chosen each year to encourage countries to improve various types of health programs. Because the emphasis this year is on food, another United Nations agency, the Food and Agriculture Organization, is co-sponsor of the day.

Training for Public Health Workers.—The Public Health Service is accepting applications from public health workers for graduate or specialized training for the 1957-1958 academic year under the special training legislation voted by Congress last July. The program is aimed at alleviating the shortage of trained personnel in various fields of public health.

In the President's budget, submitted Jan. 16, 2 million dollars is requested for the program in the fiscal year 1958 to give additional training to physicians, sanitary engineers, nurses, and other professional personnel now working in public health or interested in entering this field.

Congress voted 1 million dollars for the first year of operation of the program, and more than 300 traineeships have been awarded, either directly by the Public Health Service or through grants to the training institutions. The recipients of these traineeships include 16 physicians, 150 nurses, 33 health educators, 25 sanitary engineers, 26 sanitarians, 11 laboratory workers, 10 dentists, and 9 veterinarians. The traineeships provide, in addition to academic costs and fees, stipends covering living expenses for the trainee and his legal dependents. Applicants should submit their applications by April 1, 1957. Information regarding the program is being made available by the Bureau of State Services, Division of General Health Services, U. S. Public Health Service.

Research on Air and Water Pollution.—The Public Health Service awarded 104 grants totaling $1,464,881 in the last six months of 1956 to support research in water pollution, water supply, and air pollution, Surgeon General Leroy E. Burney has announced. Seventy-four of these grants, totaling $713,972, are for research in water supply and water pollution, 36 being for new projects, and 38 for projects already under way. These grants include awards to investigators in 43 institutions in 27 states and the District of Columbia. Thirty grants, totaling $750,909, are for research in problems of community air pollution. These grants were distributed among investigators located in 24 institutions in 14 states.

The grants are awarded on recommendation of the National Advisory Health Council, and are administered by the National Institutes of Health. Information on these grants, including the names of investigators, institutions, and amount of support, may be obtained from the Division of Sanitary Engineering Services, Bureau of State Services, U. S. Public Health Service, Washington 25, D. C.

Personal.—Dr. Victor Haas, director, National Institute of Allergy and Infectious Diseases, will return in April to laboratory research at the institute in the field of microbiology. He will be succeeded by Dr. Justin M. Andrews, now associate chief for program in the Public Health Service bureau of state services.

DEATHS

Finn, Herbert George ✱ West Medford, Mass.; born in Malden Nov. 1, 1907; Harvard Medical School Boston, 1932; certified by the National Board of Medical Examiners; specialist certified by the American Board of Surgery; clinical instructor in surgery at Tufts College Medical School, Boston; member of the Industrial Medical Association; fellow of the American College of Surgeons; veteran of World War II; medical director of the H. P. Hood Company; served on the staffs of the Soldiers' Home in Chelsea, Danvers State Hospital in Danvers, Sancta Maria Hospital and Holy Ghost Hospital for the Chronically Ill in Cambridge, St. Elizabeth's and Carney hospitals in Boston, and the Lawrence Memorial Hospital in Medford, where he died Nov. 13, aged 49, of cancer of the liver and pancreas.

Boyd, Douglas ✱ Highland Park, Ill.; born in Griffin, Ga., Feb. 22, 1898; Harvard Medical School, Boston, 1922; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the Institute of Medicine of Chicago and the Chicago Society of Internal Medicine; past-president of the Lake County Medical Society; served as president of the board of health of Highland Park; at one time on the faculty of Northwestern University Medical School in Chicago; veteran of World Wars I and II; on the staffs of the Lake Forest Hospital, Lake Forest, and the Highland Park Hospital, where he was formerly chief of medical service and where he died Dec. 21, aged 58.

Ohly, John Henry ✱ Brooklyn, N. Y.; born in Brooklyn in 1877; Long Island College Hospital, Brooklyn, 1899; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology, American Ophthalmological Society, and the Association for Research in Ophthalmology; fellow of the American College of Surgeons; on the staffs of the Brooklyn Eye and Ear Hospital and Caledonian Hospital; consultant at the Kings County, Swedish, St. John's Episcopal, Long Island College, Brooklyn Thoracic, and Wyckoff Heights hospitals and the Norwegian Lutheran Deaconess Home and Hospital; died in the Brooklyn Hospital Dec. 13, aged 79, of cerebral hemorrhage.

Hinkel, Charles Luther ✱ Danville, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1936; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, Radiological Society of North America, and the American College of Radiology, of which he was a counselor; on the staff of the George F. Geisinger Memorial Hospital and Foss Clinic; served during World War II and was awarded the Bronze Star medal for outstanding accomplishments; died Dec. 10, aged 46, of coronary disease.

✱ Indicates Member of the American Medical Association.

Josephi, Marion Gertrude, Walnut Creek, Calif.; Cornell University Medical College, New York City, 1926; an associate member of the American Medical Association; member of the American Academy of Pediatrics; certified by the National Board of Medical Examiners; specialist certified by the American Board of Pediatrics; veteran of World War II; served with the county health department and as director of the rheumatic fever program of the state department of public health; died Dec. 5, aged 55, of carcinoma of the breast with metastases.

Lien, Arthur Edward ✱ Spokane, Wash.; born in Black River Falls, Wis., July 20, 1891; Northwestern University Medical School, Chicago, 1926; fellow of the American Public Health Association and the American College of Surgeons; past-president of the Spokane County Medical Society and the Spokane Surgical Society; county health officer and director of health for Spokane School district no. 81; served as county physician, coroner, and deputy coroner; on the staffs of the Sacred Heart and Deaconess hospitals; died Nov. 29, aged 65, of arteriosclerotic heart disease.

Madigan, John Joseph ✱ Colonel, U.S. Army, retired, Washington, D. C.; born in Washington June 30, 1879; Georgetown University School of Medicine, Washington, 1909; veteran of World War I; formerly professor of military science and tactics at his alma mater; retired June 30, 1941; during World War II served as personal physician to General George C. Marshall; later member of the retirement board at the Walter Reed General Hospital; specialist certified by the American Board of Psychiatry and Neurology; died Dec. 7, aged 77, of a heart attack.

Berk, M. David ✱ Pompton Lakes, N. J.; State University of Iowa College of Medicine, Iowa City, 1932; specialist certified by the American Board of Preventive Medicine; veteran of World War II; served as school physician, member of the board of health, and police surgeon; on the staff of the Chilton Memorial Hospital, Pompton Plains; a member of the advisory board of the Pompton Lakes Branch of the First National Bank of Paterson; died in Washington, D. C., Dec. 9, aged 48.

Hennerich, Walter Emil, St. Louis; St. Louis University School of Medicine, 1916; assistant professor of clinical surgery at his alma mater; fellow of the American College of Surgeons; veteran of World War I; since 1949 hospital commissioner of St. Louis; on the staffs of St. Mary's, Firmin Desloge, and St. Louis City hospitals; in 1945 was awarded a plaque for distinguished service to the city's hospitals by the alumni of the St. Louis City Hospital; died in De Paul Hospital Dec. 3, aged 65, of congestive heart failure.

Akers, William Oldman, Covina, Calif.; John A. Creighton Medical College, Omaha, 1902; veteran of World War I; died Sept. 24, aged 82.

Baer, Adolph ✱ Brooklyn, N. Y.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1928; member of the American College of Gastroenterology; on the staffs of the Kings County and Unity hospitals; died Dec. 7, aged 51, of coronary thrombosis.

Bassett, Louis Herbert, Seattle; Rush Medical College, Chicago, 1941; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World War II; formerly practiced in Detroit; a psychiatrist at the mental hygiene clinic of the Veterans Administration regional office; died in Shelton Dec. 1, aged 48.

Bennion, Theron Wilson ✱ Port Chester, N. Y.; University of Pennsylvania School of Medicine, Philadelphia, 1922; died in the United Hospital Dec. 12, aged 67.

Bluestone, Moses Abraham, Brooklyn, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1920; on the staff of the Coney Island Hospital; died in the Long Island College Hospital Dec. 20, aged 61, of coronary thrombosis.

Budke, Robert Julius ✱ St. Charles, Mo.; Washington University School of Medicine, St. Louis, 1935; veteran of World War II; on the staff of St. Joseph's Hospital, where he died Nov. 26, aged 48, of coronary disease.

Campbell, Novel Walter, Wills Point, Texas; Kentucky School of Medicine, Louisville, 1894; veteran of World War I; died in the Veterans Administration Hospital, McKinney, Dec. 10, aged 84, of cerebral hemorrhage.

Campbell, William Breaden, Orlando, Fla.; Jefferson Medical College of Philadelphia, 1906; served on the staffs of the Grove City (Pa.) Hospital and the Butler (Pa.) County Memorial Hospital; died Dec. 28, aged 86, of cerebral thrombosis and arteriosclerosis.

Carne, John Emerson ✱ Dyersburg, Tenn.; University of Tennessee College of Medicine, Memphis, 1947; secretary-treasurer of the Dyer, Lake and Crockett Counties Medical Society; veteran of World War II; served in the Korean War; died Nov. 27, aged 42, of myocardial infarction.

Carr, Frank Clyde, East Hampton, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1913; specialist certified by the American Board of Otolaryngology; served on the staffs of the New York Eye and Ear Infirmary and the Doctors Hospital in New York City; died in the Central Islip State Hospital, Central Islip, Dec. 13, aged 69, of paralysis agitans and cerebral arteriosclerosis.

Casey, Albert Harvey ✱ Utica, N. Y.; University and Bellevue Hospital Medical College, New York City, 1919; member of the staff of St. Elizabeth Hospital; died Dec. 17, aged 63, of carcinoma of the fundus of the stomach.

Clark, William Frederick ✱ New Castle, Pa.; Eclectic Medical College, Cincinnati, 1924; died in the Jameson Memorial Hospital Sept. 14, aged 67.

Cohn, Franklin, New York City; University of Pennsylvania Department of Medicine, Philadelphia, 1905; veteran of World War I; died in the Veterans Administration Hospital Nov. 2, aged 73, of myocardial infarction and paralysis agitans.

Collins, James Cleveland, Fairmont, W. Va.; George Washington University School of Medicine, Washington, D. C., 1909; an associate member of the American Medical Association; past-president of the Marion County Medical Society; on the staff of the Fairmont General Hospital, where he died Dec. 22, aged 72, of arteriosclerotic cardiovascular renal disease.

Copulsky, Louis, Brooklyn, N. Y.; Universität Bern Medizinische Fakultät, Switzerland, 1936; member of the Medical Society of the State of New York; veteran of World War II; on the staffs of Madison Park Hospital of Adelphi College and Coney Island Hospital; died Dec. 14, aged 46, of coronary sclerosis.

Couper, Edgar Ward, San Francisco; College of Physicians and Surgeons of San Francisco, 1899; served on the staff of St. Francis Memorial Hospital, where he died Dec. 23, aged 94, of arteriosclerosis.

Crain, L. Frank ✱ Deep River, Iowa; Rush Medical College, Chicago, 1900; died Jan. 6, aged 83, of pneumonia.

Dorman, Joseph Harold ✱ Dallas, Texas; Baylor University College of Medicine, Dallas, 1912; member of the founders' group of the American Board of Surgery; served on the faculty of his alma mater and the Southwestern Medical School of the University of Texas; served with the British and American armies during World War I; on the staffs of St. Paul's Hospital and the Baylor University Hospital; died Dec. 7, aged 67, of acute coronary insufficiency.

Douglass, James Edgar, Jr., Winnsboro, S. C.; Medical College of South Carolina, Charleston, 1917; died in the South Carolina Baptist Hospital, Columbia, Nov. 17, aged 65, of coronary thrombosis.

Dubbe, Frederick Henry ✱ New Ulm, Minn.; University of Minnesota Medical School, Minneapolis, 1920; fellow of the American College of Surgeons; on the staffs of the Loretto and Union hospitals; died Nov. 30, aged 61, of coronary occlusion.

Dunnington, Ruel Norman ✱ Benton Harbor, Mich.; Northwestern University Medical School, Chicago, 1909; served on the board of education; past-president of the Berrien County Medical Society; member and past-president of the Benton Harbor Exchange Club; died Dec. 6, aged 74, of a heart attack.

Ferrier, William Henry, Watkins Glen, N. Y.; Jefferson Medical College of Philadelphia, 1905; an associate member of the American Medical Association; died in the Schuyler Hospital, Montour Falls, Oct. 2, aged 75, of ruptured aneurysm of the aorta.

Flynn, John Molloy ✱ Boston; Harvard Medical School, Boston, 1927; specialist certified by the American Board of Internal Medicine; fellow of the American

College of Physicians; on the faculty of his alma mater; member of the state board of registration in nursing; served on the staffs of St. Elizabeth's and Peter Bent Brigham hospitals; physician-in-chief at Cambridge City Hospital, Cambridge; died in Belmont Dec. 11, aged 57, of coronary disease.

Ford, Charles Wesley, Springfield, Mo.; Sioux City (Iowa) College of Medicine, 1900; died Oct. 16, aged 89.

Foster, Anthom Ackward, Los Angeles; Meharry Medical College, Nashville, Tenn., 1921; died in the Temple Hospital Nov. 23, aged 67, of cerebral hemorrhage, hypertension, and arteriosclerosis.

Foy, James Woodward * Seymour, Texas; Baylor University College of Medicine, Dallas, 1926; member of the American Academy of General Practice; on the staff of the Baylor County Hospital, where he died Dec. 10, aged 55, of pulmonary embolus.

Fraser, Robert Carson * Los Angeles; Detroit College of Medicine, 1905; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; on the staffs of St. Joseph Hospital in Burbank and the Presbyterian Hospital–Olmsted Memorial; died Dec. 13, aged 72, of carcinoma of the esophagus.

Garrard, John Lucius * Rome, Ga.; University of Georgia Medical Department, Augusta, 1907; twice president of the Floyd County Medical Society; served as president of the Georgia Urological Society; on the staffs of the McCall and Floyd hospitals; died Dec. 4, aged 75, of congestive heart disease.

Gerrard, Clarence Charles * Bakersfield, Calif.; University of Vermont College of Medicine, Burlington, 1913; formerly practiced in Redding, where he was president of the Shasta County Medical Society; on the staffs of the Kern General Hospital and the Mercy Hospital, where he died Dec. 11, aged 67, of a heart attack.

Gibbes, Robert W. * Columbia, S. C.: Medical College of South Carolina, Charleston, 1895; died Dec. 10, aged 84.

Gideon, Simon D. * Chicago; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1923; fellow of the International College of Surgeons and the American College of Gynecology and Obstetrics; on the courtesy staffs of the Woodlawn, American, and Edgewater hospitals and the Michael Reese Hospital, where he died Dec. 15, aged 59, of cancer.

Golden, John Henry * San Francisco; Georgetown University School of Medicine, Washington, D. C., 1930; member of the American Academy of General Practice; member of the executive committee and board of trustees at Mary's Help Hospital; died in Boise, Idaho, Dec. 18, aged 50, of auricular fibrillation and arteriosclerosis.

Hall, William Shepherd, Baltimore; University of Maryland School of Medicine, Baltimore, 1899; an associate member of the American Medical Association; served on the staffs of the University and Johns Hopkins hospitals; died in the Union Memorial Hospital Nov. 25, aged 80, of acute myocardial infarction.

Hanna, Edward Alexander, Philadelphia; Temple University School of Medicine, Philadelphia, 1934; an associate member of the American Medical Association; veteran of World War II; on the staff of the Presbyterian Hospital; died in Wynnewood Dec. 9, aged 48, of coronary infarct.

Harriss, Andrew Howell * Wilmington, N. C.; Medico-Chirurgical College of Philadelphia, 1893; veteran of the Spanish-American War and World War I; died Nov. 24, aged 84, of coronary disease.

Heller, Alexander John * Ridgewood, N. Y.; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1916; died in the Evangelical Deaconess Hospital, Brooklyn, Dec. 5, aged 62, of cerebral hemorrhage and arteriosclerosis.

Henry, George Linwood, New York City; Howard University College of Medicine, Washington, D. C., 1925; veteran of World War I; died in the Bellevue Hospital Nov. 15, aged 56, of hepatic cirrhosis and gastrointestinal hemorrhage.

Hogg, Robert Letcher, Saratoga, Calif.; University of Louisville (Ky.) Medical Department, 1893; chairman of the advisory board of the Los Gatos Bank of America; died Nov. 29, aged 83.

Hopkins, John Edward * Detroit; University of Toronto Faculty of Medicine, Toronto, Canada, 1923; on the staff of the Lincoln Hospital, where he died Nov. 26, aged 59, of acute coronary thrombosis.

Hughes, John Cecil, Brooklyn, N. Y.; New York Homeopathic Medical College and Hospital, New York City, 1913; died Dec. 19, aged 70, of arteriosclerotic heart disease.

Jacobs, David Clark, Three Rivers, Mich.; Wayne University College of Medicine, Detroit, 1953; since April 1, 1955, an officer in the U.S. Army Reserve; died near Buena Vista, Colo., Sept. 24, aged 28, in an aircraft accident.

Kellogg, Henry Kirke White * Norwalk, Conn.; Columbia University College of Physicians and Surgeons, New York City, 1903; served as chief of surgery at the Norwalk Hospital; vice-president of the Fairfield County Savings Bank; died Dec. 5, aged 80, of coronary heart disease.

Kenner, Lucy Alice, Buffalo; University of Buffalo School of Medicine, 1911; died Nov. 28, aged 78.

Kingston, Elwood Almon * Lockport, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; fellow of the American College of Surgeons; for many years county coroner; served as director of the First National Bank;

on the staffs of the St. Joseph's Hospital and the Silver Cross Hospital in Joliet, where he died Nov. 20, aged 80, of gastrointestinal hemorrhage due to duodenal ulcer.

Kish, Paul A., Franklin, Ga.; Eastern University School of Medicine, Baltimore, 1913; died in the Emory University Hospital, Emory University, Nov. 28, aged 69, of carcinoma of the lung.

Knight, Edwin Graham ✱ Swanville, Minn.; University of Minnesota Medical School, Minneapolis, 1940; member of the American Academy of General Practice; died in Mounds Park Hospital, St. Paul, Nov. 29, aged 42.

Knudson, Knute Otto, Glenburn, N. D.; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1903; veteran of World War I; died in Minot Nov. 22, aged 77.

Koch, Ernst H. ✱ Louisville, Ky.; Kentucky University Medical Department, Louisville, 1900; served on the staffs of the SS. Mary and Elizabeth Hospital and St. Anthony's Hospital, where he died Dec. 3, aged 78, of a skull facture received in a fall.

Kurbitz, Kenneth Woodrow ✱ Yakima, Wash.; Georgetown University School of Medicine, Washington, D. C., 1941; veteran of World War II; on the staffs of the St. Elizabeth Hospital and the Yakima Valley Memorial Hospital, where he died Nov. 28, aged 49, of coronary occlusion.

Lawlor, James Joseph, Cambridge, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1920; member of the Massachusetts Medical Society; on the staff of the Otis General Hospital; died Dec. 4, aged 62, of carcinoma of the prostate.

Lawson, George William ✱ Graham, N. C.; Long Island College of Medicine, Brooklyn, N. Y., 1935; member of the American Academy of General Practice; veteran of World War II; died in the Veterans Administration Hospital, Durham, Dec. 3, aged 53.

Lax, Morris H. ✱ St. Paul; University of Minnesota Medical School, Minneapolis, 1923; member of the American Academy of General Practice; on the staff of the Bethesda Hospital, where he died Nov. 21, aged 62.

Laymon, Russell Lowell, Miami, Fla.; University of Michigan Medical School, Ann Arbor, 1930; killed Nov. 9, aged 51, in an automobile accident.

Lemmon, Harry Jacob, Newport, Tenn.; University of Louisville (Ky.) Medical Department, 1916; died Dec. 4, aged 67.

Levine, George Irving ✱ Jersey City, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1930; veteran of World War II; on the staff of the Fairmount Hospital; died Dec. 2, aged 53, of coronary occlusion.

McKay, Beatrice A. Smith, Niagara Falls, N. Y.; University of Buffalo School of Medicine, 1924; member of the Medical Society of the State of New York; died in Mount St. Mary's Hospital Oct. 16, aged 56, of an embolus at the bifurcation of the abdominal aorta, with gangrene.

Manning, George Washington, Lynbrook, N. Y.; Temple University School of Medicine, Philadelphia, 1908; died in the Veterans Administration Hospital, Aspinwall, Sept. 14, aged 81.

Merideth, John Andrew ✱ Cobden, Ill.; Washington University School of Medicine, St. Louis, 1927; president of the Union County Medical Society; fellow of the American College of Surgeons; veteran of World War II; on the staffs of the Metropolis Memorial Hospital in Metropolis and the Union County Hospital in Anna, where he died Sept. 27, aged 55, of coronary arteriosclerosis.

Monaghan, Hugh John ✱ Hamburg, N. Y.; University of Toronto Faculty of Medicine, Toronto, Canada, 1925; died Dec. 28, aged 59.

Norris, George Henry, Annandale, Minn.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; veteran of World War I; died Nov. 27, aged 86, of a skull fracture received in a fall down the stairs.

Pulliam, Madison James ✱ St. Louis; St. Louis University School of Medicine, 1912; fellow of the American College of Surgeons; veteran of World War I; served on the faculty of his alma mater; on the staffs of St. Mary's Group of Hospitals and St. Anthony's Hospital, where he died Dec. 15, aged 70, of lymphatic leukemia.

Pumphrey, J. Homer ✱ Clayton, Ohio; Starling Medical College, Columbus, 1901; on the staff of the Good Samaritan Hospital, Dayton, where he died Nov. 17, aged 83, of uremia.

Russell, Charles C., Resaca, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1909; died in Calhoun Dec. 2, aged 83.

Senter, John Thomas, Fulton, Miss.; Louisville (Ky.) Medical College, 1907; served as county health officer; recipient of the Itawamba County Distinguished Citizenship Award in 1947; died Dec. 22, aged 78.

Smith, Grover Allen ✱ New Haven, Ind.; Eclectic Medical College, Cincinnati, 1911; veteran of World War I; served as county coroner; on the courtesy staff of St. Joseph Hospital in Fort Wayne; on the honorary staff of the Lutheran Hospital and Parkview Memorial Hospital in Fort Wayne, where he died Nov. 17, aged 71, of cerebral embolism.

Williamson, William Harvey ✱ Mokane, Mo.; Kentucky School of Medicine, Louisville, 1893; died Nov. 16, aged 88.

Wood, Hiram D., Minneapolis; the Hahnemann Medical College and Hospital, Chicago, 1897; died in St. Peter State Hospital, St. Peter, Dec. 21, aged 85, of myocardial degeneration and arteriosclerosis.

FOREIGN LETTERS

ARGENTINA

Medical Education.—In 1956, the administration of medical schools was in the hands of provisional authorities. Different committees were formed for the selection of full professors from among the available applicants. By Jan. 1 all the professors in the medical school of Buenos Aires had been appointed. The dean and the members of the council will be selected in 1957. No changes were made with regard to the admission of students. The 6 medical schools have a total registration of 27,790 students, as compared with 28,160 in the 85 schools in the United States. As there was no limitation in the medical school of Buenos Aires, 4,200 students were accepted for the first year, but, of these, 60% dropped out before finishing the first year. A preparatory course has been established in the Buenos Aires medical school to improve the quality of the applicants. In 1940, 43% of the first-year students finished their medical course. The corresponding percentages were 32 in 1950 and 18 in 1955.

AUSTRIA

Ethyleneimine Quinone.—At the meeting of the Vienna Medical Society on Dec. 14, E. E. Reimer reported his experience with ethyleneimine quinone (E 39) in treating 20 patients, 10 of whom had neoplasia of different kinds and 10 of whom had lymphocytic leukemia, myeloblastosis, lymphogranuloma, or plasma cell myeloma. Disorders of granulopoiesis were treated with large doses of the drug. Oral or intravenous administration of it did not alleviate conditions of tumors or their metastases, but marked decrease in the number of cells and regression of the symptoms occurred after injections were given directly into the tumor. The drug also produced a temporary maturation of cells in patients with myeloblastosis, but no improvement was noted in patients who had received inadequate treatment for lymphogranulomas or in those whose condition had been resistant to therapy. A definite albuminosis occurred in patients with plasma cell myeloma when the globulins were reduced. The speaker cautioned against uncontrolled treatment with the drug because of the danger to the hemopoietic system.

H. Holzner reported that at autopsy a series of 13 patients who had been treated with E 39 showed no morphologic influences of the drug on granulocytic leukemia and lymphadenosis. There were, however, excessive fatty degeneration and polymorphism of the tumor cells, extensive necrosis, and fibrosis. Severe bone-marrow lesions, which in some cases lead to a total atrophy of the blood-forming tissue, were also noted. Such changes cannot be considered as specific effects of the drug. It cannot yet be said whether E 39 is an improvement over other cytostatic agents in the therapy of malignant blastomas.

A. Pillat reported on five patients with tumors on the eyelids treated locally with E 39. Two patients had epithelioma, two melanoma, and one an inflammatory chalazion on the lid margin. A quick regression of the two epitheliomas occurred within 10 and 12 days respectively. One of the melanomas became necrotic and the other shrank to half its former size. No similar response was observed in the chalazion. The short period of observation (four weeks) does not allow an evaluation of the final results. General treatment with E 39 is not recommended.

H. Kretz and Hinterberger reported that of 30 patients who had various types of inoperable malignant tumor and who were treated with E 39 no improvement was observed in 15 (2 of whom were practically moribund when the treatment was started and 3 of whom had melanosarcoma), but on autopsy the tumors showed evidence of regressive changes. Therapy had to be discontinued in 5 patients, and in 10 the general condition of the patient improved, the tumors shrank, there was no recurrence of ascites, and the pain subsided. The results were especially favorable when it was possible to inject the drug directly into the tumor. E 39 was injected into residual tumors during radical operations in other patients. No cures have been effected with the drug.

J. Kretz stated that chemotherapy with E 39 may be hazardous not only because of the toxicity of the drug but also because of the toxicity of the disintegration products of the tumor. Local therapy appears to be more successful than systemic therapy. E 39 may be injected through the portal vein into hepatic tumors, through the femoral artery into tumors of the limbs, or through the internal carotid artery into tumors of the brain.

K. Prausmüller stated that a carcinomatous pleuritis was controlled by giving 25 mg. of E 39 intravenously every day. The pleuritis appeared after ablation of a carcinomatous breast three years earlier. Süss reported on 13 patients who were treated with E 39. Two had bronchogenic carcinoma with an extension of the cancer tissue into the trachea. An intratracheal removal was performed on both patients because of the danger of suffocation, and treatment with E 39 was started. The drug was given intravenously and by inhalation. It cannot be incorporated in an aerosol, because it is unstable in solution. Stridor and danger of suffocation disappeared three or four months after treatment was started.

R. Bauer stated that he had given E 39 only to patients with inoperable tumors. His series included seven patients with carcinoma and three with sarcoma of the larynx. No improvement was observed when the drug was given intravenously, but remarkable improvements followed local applications. The hard, compact

The items in these letters are contributed by regular correspondents in the various foreign countries.

lymph nodes in the throat increased rapidly in size, then softened in the center. Large amounts of necrotic matter were evacuated from these abscesses. Histologically the abscess walls showed an intensely inflammatory infiltration, which in some locations penetrated the surrounding musculature. In some patients these tissues were completly free from carcinomatous elements. Single aggregations of cancer cells, which showed clearly regressive changes, were found in some specimens. Extensive fibrosis was observed. It is not yet known what dose is necessary to destroy the tissue of a tumor without damaging the normal tissue. Too extensive necrosis may cause a fatal toxic reaction analogous to that seen after x-ray therapy. E 39 has the advantage that it may be used for a long time. Small doses given over a long period are probably less dangerous and more efficacious than larger doses given over a shorter period.

Treatment of Brain Tumors with Radioactive Cobalt.—At the same meeting D. W. Kruger of Ischl stated that, although both surgical and x-ray treatment for cerebral spongioblastomas has up to now been unsuccessful, irradiation with radioactive cobalt (Co^{60}) directly into the tumor has given good results. After surgical removal of the tumor, the Co^{60} should not be introduced until the wound is completely healed (in order to prevent an irradiation burn) and should be removed after 20 or 24 hours. In this time about 6,500 r may be applied. In a series of seven patients so treated, remarkable improvement of the general condition and prolongation of the survival time was observed.

BRAZIL

Intrapericardial Anatomy.—Drs. Ugo Pinheiro Guimarães and Felipe Sayeg reported in *Revista brasileira de cirurgia* (**31**:577, 1956) on the examination of the pulmonary hili of 50 cadavers. The permeability of the vestigial fold was examined in 22 cadavers, in 19 of which there was no patency. In all three cases in which there was patency the absence of blood was ascertained. A common pulmonary vein was found in 11 patients, in 3 on the right side and in 8 on the left. The place of formation of this common pulmonary vein was found to be intrapericardial in two patients, extrapericardial in two, and in the extremity of the pericardial sac in seven. The number of patients with vessels in the interior of the pericardium was as follows: superior pulmonary vein on the right side in 40 and on the left in 40 also; inferior pulmonary vein on the right side in 25 and on the left in 40; and common pulmonary vein on the right side in 3 and on the left in 8. The authors found other anomalies, including two azygous lobes and two veins of the upper lobe draining the superior vena cava.

Incidence of Puerperal Eclampsia.—Drs. Sergio Yazbek and Vasco F. Almeida of the São Paulo Maternity Hospital reported on the incidence of puerperal eclampsia in a series of 113,309 deliveries. In this group, 414 cases of puerperal eclampsia occurred (0.38%), 300 in indigent patients (0.58%) and 114 in paying patients (0.18%). Grouped by age, 115 (27.7%) of the patients were 10 to 19 years of age, 232 (56.0%) were 20 to 29, 57 (13.7%) were 30 to 39, and 10 (2.5%) were 40 to 49. As to the duration of gestation when eclampsia occurred, 4.4% occurred at between six and one-half and seven and one-half months, 11.7% at between seven and one-half and eight and one-half months, and 71.6% at between eight and one-half and nine months; for 12.3% the duration of gestation was not given. Primiparas accounted for 269 cases (65%) and biparas for 62 (15%), the percentage tapering off regularly as the multiparity of the mother increased. In 188 cases (45.5%) the infant was a boy and in 226 (54.5%) it was a girl. During the 16-year period of the study, the incidence of puerperal eclampsia decreased: In the first year (1940), 0.8% of the deliveries were complicated by eclampsia, 0.5% for the paying women and 1.1% for the indigent; in 1955 only 0.03% of the group that paid and 0.26% of the group that was indigent had such complications.

Psychotic Constitution of the Brain.—Prof. Walter E. Maffei of São Paulo at a meeting of the Associação Paulista de Medicina reported on the anatomic bases of the psychotic constitution of the brain. Having examined a great number of brains of psychotic and healthy persons, he observed several anomalies in the former. The most evident were changes in the shape of the brain and its lobes, the persistence of the sylvian fossa or fossa lateralis, the presence of anomalous fissures, and the closure of the anterior part of the sylvian fissure. He emphasized that these embryogenic alterations do not represent the pathological substratum of psychosis, nor are they specific for a particular psychosis. Rather they constituted only the morphologic elements of the psychotic constitution of the brain. Only in epilepsy does one observe pathognomonic changes (hypoplasia of one of the hemispheres, mainly evidenced in the cornu Ammonis, accompanied by similar changes in such other formations as the trigone, thalamus, olfactory nerves, and temporal lobes). Thus, examination of the brain permits the diagnosis of epilepsy even in the absence of history of convulsions.

Tetanus.—At the same meeting, Dr. D. Pinheiro of the São Paulo State University Hospital reported that the case fatality rate for tetanus (umbilical tetanus not included) before the use of mephenesin as an adjunct to other therapeutic measures was 37.5%. This figure fell to 24.5% with the introduction of the relaxant drug and represents one of the lowest rates reported. The case fatality rate for umbilical tetanus, which was 92.5%, fell to 77.3% after the use of mephenesin.

CANADA

Railroads Buy Health and Welfare Benefits.—After months of negotiation, the railroad companies and the unions representing employees agreed on a comprehensive health and welfare program for employees and dependents, which became effective on Jan. 1. This is the biggest program of its kind ever negotiated in Canada. It was negotiated by the medically sponsored,

nonprofit voluntary health plans in the provinces through their two Dominion representatives, Trans-Canada Medical Plans and the Canadian Council of Blue Cross plans. In addition to basic hospital expense protection for 70 days at standard ward rates and surgical and medical benefits, there are group life insurance, with a $500 per employee coverage, and a weekly indemnity of $40 in cases of sickness or non-occupational disease. The group-life and weekly benefits were negotiated separately by a syndicate of Canadian life insurance companies. There will be a payroll deduction of $4.25 a month, and this will be matched by an equal contribution from the employer. The present contract is of two years' duration. A distinction was made between the provinces, such as British Columbia, Alberta, and Saskatchewan, where government hospital schemes already exist and those in which there is no such provision. In the former the basic benefits will not include hospital coverage, but the full amount of money available for health services will be used for comprehensive medical coverage.

Provision is made for the employee voluntarily to purchase additional coverage on a payroll deduction basis if he so desires. One point that has been raised in connection with this contract is the question whether medical care can or should be split up in prepaid health insurance. Is it, for example, desirable to sell coverage for surgical work and not for care by internists? It is clear that certain administrative difficulties will arise. If, for example, a man is admitted to the hospital with a fracture, for which he is covered, and contracts pneumonia, what would the position be as regards payment for the latter? Nevertheless, it will be realized that lack of available funds in the welfare program makes it impossible to give complete coverage, although an existing plan can always be added to when economic circumstances permit.

Chamber of Commerce Opposes Health Plan.—Wide publicity has been given to a brief published by the Canadian Chamber of Commerce, in which it expresses opposition to the federal government's hospital insurance proposals. In its annual recommendations to the cabinet, the Chamber of Commerce said that such a plan would lead inevitably to compulsory health insurance of a comprehensive nature and to state medicine. It believes that any financial assistance provided by the government should be directed to areas in which the individual is generally unable to help himself, to the indigent, the aged, the chronically ill, and those who suffer catastrophic medical expenses. The Chamber of Commerce represents more than 750 boards of trade, and in its brief it urges that active government participation in business and international trade be kept to a minimum. It points out that so-called free health services will result in vastly increased demands for such services and that the cost of a compulsory and comprehensive national health program will be substantially more than present health expenditures in Canada. "In a free society, the individual has the primary responsibility to make provision for and pay the cost of medical care for himself and family." Encouragement and aid from employers should be given to voluntary prepaid medical care plans, which are already covering a substantial proportion of the population.

Emotional Factors in Thyrotoxicosis.—Thyrotoxicosis tends to recur in spite of apparently adequate treatment. Ferguson-Rayport (*Canadian Medical Association Journal*, Dec. 15) studied 20 patients with thyrotoxicosis in order to assess the role of emotional factors in recurrence and, thereby, to devise a more predictable management of the disease. In the present group, 10 patients were undergoing their second attack of thyrotoxicosis and 10 were in good health 12 to 18 months after treatment of a first attack. The author believes that initial and subsequent attacks are understandable if the patient's feelings, behavior, and conflictive situation are considered along with the physiological changes. Patients fall into three categories: (1) those responding rapidly to somatic treatment and relapsing only under major stress; (2) those in whom a toxic condition reappears on the slightest provocation; and (3) those with bursts of thyroid hyperactivity under stress but with spontaneous remission. The variability of response is related to ability or inability to achieve emotional equilibrium concurrent with the somatic treatment. The unsatisfactory therapeutic results are linked with failure of the physician to understand his patient's lifelong patterns of reactions, possible modes of adaptation, and subjective experience of the illness. This does not imply that a psychiatrist should help treat the patient; the same family physician should learn to deal with psychological and somatic aspects of the case.

L. E. Cell Reaction.—The L. E. cell reaction is a well-known in vitro phenomenon observed when plasma, serum, or serous effusions from patients with acute disseminated lupus erythematosus are left in contact with fresh white cell elements of blood or bone marrow. M. A. Ogryzlo (*Canadian Medical Association Journal*, Dec. 15, 1956) used most of the methods previously described but did most of his tests with clotted venous blood that had stood at 21 or 37 C for two hours. He carried out 1,250 tests on 750 patients suffering from a variety of diseases other than acute disseminated lupus but such as to suggest that a positive test might be obtained. He showed that the most significant feature of the L. E. cell reaction in vitro is an unusual type of degeneration affecting some of the white cells of blood or marrow in the presence of the L. E. cell factor, with lysis and release of their nuclei. Some of the amorphous nuclear masses thus released were ingested by phagocytic leukocytes to form L. E. cells. All white cells in peripheral blood may take part in the reaction. The L. E. cell phenomenon may be demonstrated in diseases other than acute disseminated lupus and may be negative in the latter. In the present study it was positive in 17 patients with rheumatoid arthritis, 3 with chronic hepatitis, and one each with scleroderma, dermatomyositis, essential polyangiitis, acquired hemolytic anemia, and Hodgkin's disease. It was also positive in two patients after reactions to phenylbutazone and in four after reactions to hydralazine. Hence L. E. cells may represent a reactive state

of the tissues associated with an abnormality of the immune mechanism that may occur in a variety of morbid states.

Books with a Medical Interest.—Toward the end of 1956 several books with a medical interest appeared in Canada. The latest, which is selling well to the general public in spite of its somewhat technical subject, is "Stress of Life" by Hans Selye. In this, Dr. Selye expounds in fairly simple language his concept of stress. He begins with a historical account of the discovery of nonspecific stress reactions and the evolution of the stress concept. He continues with a much more difficult section on the general and local adaptation syndromes, the relation of stress to inflammation, and the nature of adaptation. He then describes the diseases of adaptation, ending with the admission that there are critics of the adaptation theory. In the next section, the general reader is again in deep water, with an outline of a unified theory of specific and nonspecific responses. Finally he describes the applications of the stress concept to daily living. This is presumably the part of the book that is attracting the general public, though they will be disappointed with the suggestion that there is no ready-made success formula that will suit everyone.

Anne Wilkinson, a descendant of the Osler family and a poetess of some note, has brought out a discursive history of the Osler family entitled "Lions in the Way." She has drawn freely on family documents and throws light on some of the lesser known facets of life among this remarkable clan. The key figure in the book is Sir William Osler's mother, who lived to be a centenarian and who gave birth to four highly successful sons—one judge, one lawyer, one physician, and one financier, whose success made some of Osler's work possible. We also encounter the inevitable black sheep of the family—one a general failure and the other a remittance man. Medical historians, professional and amateur, should welcome this book.

The third book that is being widely read is a study by three social scientists of life in a prosperous community in the most sought-after area of a Canadian metropolis. "Crestwood Heights," the title of the third book, is a thinly disguised name for an opulent section of Toronto, and the three authors dissect with skill its structure, institutions, function, and beliefs. This book proves, among other things, that social scientists can write fascinating books in excellent prose. The account is put together from investigations voluntarily submitted to by the inhabitants of Crestwood Heights. It should give much food for thought to the person practicing individual psychiatry and to the social psychiatrist. Some readers will be utterly appalled at the picture revealed of complete materialism. Others will approve the efforts of this dedicated and committed community, all believing that they are the masters of their own fate and all "subscribing to the great North American dream of a material heaven in the here and now to be entered by the successful elect." This study grew out of a project to learn more about child growth in a comparatively homogenous and prosperous urban and suburban environment. It was originally part of a national mental health project put forward by the National Committee for Mental Hygiene of Canada. It is to be hoped that some of the conclusions of the study are not quite representative of the community. For example, the authors say that in Crestwood Heights a man is judged largely by the number and quality of things he owns, which must be seen, approved, and envied by other men. "Adults view religion as a means to other and more important ends, such as 'happiness' or mental health." The tragedy of it all is that, though life in the Heights is anything but nasty, brutish, and short, the mental health of the population seems to be not sensibly better than anywhere else. It does not take a sociologist to tell them why—the prophets of old understood these things!

INDIA

All-India Medical Conference.—The All-India Medical Conference at Trivandrum in December urged the central and state governments to prohibit, in the interest of public health, practitioners of the Ayurvedic and Unani systems from using modern scientific drugs and from practicing modern surgery, obstetrics, and gynecology. Unless such a step is immediately taken, the object of having separate councils of registration of different systems will be defeated. The conference also warned the public against the danger of accepting from practitioners of indigenous systems and from unqualified people prescriptions and supplies of modern drugs. The conference urged the creation of a commission for awarding medical education grants. It also recommended that the government appoint expert committees to advise it on the formulation and implementation of five-year plans in relation to the health services, so that balanced planning, continuity of policy, and the most economic use of public funds could be insured. It requested the governments to include a representative of the Indian Medical Association in such committees. The state governments were urged to amalgamate medical and public health departments. The head of this unified department should also be the secretary to the Ministry of Health of the state.

Dental Clinic.—A prosthesis dental clinic was opened at the St. George's Hospital, Bombay, in December, by the Bombay Minister for Public Health, who said that, although India required nearly 9,000 dentists, there were only about 1,000 in the country. An expansion of the facilities for dental care is a part of the second Five Year Plan. To bring the service within reach of the common man, the prices charged will be the lowest anywhere in the world.

Miliary Tuberculosis.—C. V. Ramakrishnan reported an analysis of 16 cases of miliary tuberculosis (*Madras Clinical Journal*, November, 1956). The average age of the patients was 29.2 years. History of contact with tuberculous persons or familial tuberculosis was conspicuously absent in these patients; 14 denied all such exposure. Old or existing pleural effusion was observed

in seven of these patients, one having bilateral effusion and the others having effusion on one side only, there being no predilection for either side. Aspiration of the exudate was not required in any of the patients, and the effusion disappeared by absorption after chemotherapy. In all the fatal cases, effusion was present. In three patients, meningitis developed, and, of these, two who had a fulminant type of infection died. Extrapulmonary lesions were observed in six patients, with lesions involving the larynx in two, a testis and epididymis in three, and the liver in one. In one patient the bacilli were demonstrated in the pus from a scrotal ulcer. The patient with hepatic lesions showed typical tubercles in the biopsy specimen. The response to treatment was not materially retarded by the presence of these complications. Six patients whose eyegrounds were examined showed no evidence of choroidal involvement. The skin reaction obtained with old tuberculin in varying dilutions appeared to have no relation to the severity of the disease. In seven patients sputum or gastric washings were positive for tubercle bacilli; six of these had evidence of progressive pulmonary tuberculosis or extrapulmonary manifestations in addition to miliary disease.

The dramatic response obtained with chemotherapy has improved the survival rate, which in the present series was 75%. Though clinical response is noticed early, restoration of normal radiologic findings takes four to six months. No radiologic evidence of calcification as a sign of healing was observed. Of the 15 patients who could be observed sufficiently long under treatment, 8 showed optimum response to chemotherapy, 3 remained refractory to treatment up to the time of analysis, and 4 died. Chemotherapy offers the best results for patients with miliary tuberculosis.

Influence of Adenocarcinoma on Body Chemistry.—S. U. Gurnani and co-workers (*Indian J. M. Sc.* **10**:11, 1956) stated that the presence of a tumor induces impaired protein metabolism in the host. Studies on the tumor-host relationship indicate that the tumor acts as a "nitrogen trap," but, since all tumors do not behave in the same way, the authors decided to investigate the influence of serial transplantations of mammary adenocarcinoma on the biochemical composition of host tissues. Spontaneously developed mammary adenocarcinoma in Dba (bar) mice was used in all the experiments. The amino acid composition of the transplantable adenocarcinoma remained constant and reproducible up to six generations. The existence of a transplantable tumor did not affect the amino acid composition of the host that was maintained on an adequate diet. The levels of nicotinic acid rose with succeeding transplants, probably indicating an increase in metabolic activity.

Need for Trained Health Workers.—At the International Seminar in New Delhi in November, the Union Health Minister said that until ignorance and poverty were overcome health standards would remain low. On an average there is only one physician for each 6,000 persons. However, since physicians are largely concentrated in towns and cities, there is really only one for each 30,000 to 50,000 persons in villages and rural areas. One of the basic problems, therefore, is the training of health workers in sufficient numbers and the devising of means for their being more evenly distributed. Various schemes for the expansion of training facilities are being pushed forward at all levels, with direct and indirect assistance from the central government. A new orientation is being presented in the training courses, so that the trainees obtain a full appreciation of the actual problems to be met in rural areas.

NORWAY

Public Health Problems.—In a survey of the events of 1956, Dr. Karl Evang, who is in charge of the public health service, noted that the epidemic diseases, including poliomyelitis, had not given much trouble and that such diseases as typhoid, diphtheria, and scarlatina had become rare. The infant mortality continued to fall in 1956, but it varied somewhat in the different countries, being highest in the far north. While tuberculosis continued to decline in the younger age groups, it showed a tendency to increase among middle-aged and older persons. The great problem within this group is placing the cured patients back at work. On the whole, employers and fellow-workers have cooperated in the rehabilitation of persons who have had tuberculosis, but Evang got the impression that the fellow-workers were apt to snub such persons, not so much for fear of infection as for fear of losing a light job they would prefer to keep for themselves. In this connection Evang urges his compatriots to learn to live shoulder to shoulder with their ailing fellow beings and to shun what he calls "institution lunacy"—a state of mind that favors dismissal of the sick to hospitals or some other institution expected to solve all health problems. Evang also noted that the incidence of syphilis continues to decline, whereas that of gonorrhea has increased.

Legal Induction of Abortion.—The appointment by the Ministry of Justice of a committee to draw up recommendations for new regulations with regard to the induction of abortion has the following background. Under the present law, only 115 abortions were induced in Norwegian hospitals in 1920. The corresponding figure for 1954 was 3,157. These 3,157 abortions corresponded to 5% of the live births in 1954. In the same year the number of criminal abortions ran into thousands, and, although accurate figures cannot be given, it is probable that some 5,300 married women and 2,000 unmarried women were the subjects of criminal abortion in 1954. The framers of the existing regulations envisaged only strictly medical indications for the induction of abortion, but in practice these indications have been much widened without any definite legal sanction. Hence there is the need for new legislation. The above-mentioned committee drafted a law governing the induction of abortion that has greatly widened the indications for it, making provision for appropriate action on ethical, sociological, and medical grounds. Abortion may thus be induced legally in connection with rape, alcoholism, housing difficulties, and other conditions that might

render the birth of a child disastrous. The decision to induce abortion must be made by two physicians, one of whom must be the operator. The operation must be undertaken in a hospital conforming to a certain standard. At a recent meeting attended by various authorities, it was pointed out that about half of the legal abortions induced at present are on psychic indications. Since such indications are vague and doubtful, it is time that the situation was clarified by a new law couched in as definite terms as possible.

Prostatic Enlargement.—In *Tidsskrift for den norske lægeforening* for Dec. 1, Dr. E. F. Hjorth has an article on the failure of the palpatory differentiation between hypertrophy and cancer of the prostate in 474 patients. The postoperative histological diagnosis was benign hypertrophy in 400 cases (84.4%) and cancer in the rest. Among the 394 patients in whom the preoperative diagnosis was benign hypertrophy, there were 28 in whom the histological examination after the operation revealed cancer. In most of these 28 patients, the cancer was of a slowly growing, small alveolar type. Among the 80 patients in whom the preoperative diagnosis was cancer, there were 34 in whom the histological diagnosis was benign hypertrophy or prostatitis. With such a high rate of preoperative errors in diagnosis, Hjorth insists that it is indefensible to subject a patient to a radical operation or prolonged hormone treatment without biopsy confirmation of the diagnosis of cancer. He admits, however, that even examination of a biopsy specimen may, under certain conditions, fail to reveal a cancer.

PORTUGAL

Hypersensitivity to Tuberculostatic Therapy.—M. Alenquer and P. Lisboa, (*Jornal do Medico*, pp. 689-753, 1956) reported the case of a tuberculous patient who had an extreme sensitivity to aminosalicylic acid, streptomycin, and isoniazid. The administration of each of these drugs, alone or in combination, caused an alarming reaction characterized by fever, exfoliative dermatitis, hepatic tenderness, and asthma. During seven months without treatment, the patient's disease progressed rapidly. The authors then tried cortisone and isoniazid, each in doses of 300 mg. daily. The allergic reactions disappeared, and in 18 months the patient recovered.

Osteomyelosclerosis.—Marques da Gama (*Jornal da Sociedade das Ciencias Medicas de Lisboa*, pp. 120-125, 1956) states that osteomyelosclerosis is rare. It is characterized by the destruction of the medullary spaces as a consequence of the fibrosis and generalized sclerosis of the cancellous tissue, with compensatory bony myelopoiesis. The illness, more frequent in women and in late adult life, has a prolonged course, beginning with such nonspecific symptoms as fatigue, loss of weight, and slight hypochromic anemia. Later there is enlargement of the liver and spleen, and roentgenograms show an increased density of the bony trabeculae, the patchy deposition of newly formed bone, and, finally, a diffuse increase in density throughout, thus making it impossible to distinguish between cortex and medulla. Sternal puncture, which may be difficult due to the fibrosis, shows an increase in megakaryocytes, plasma cells, and lymphocytes. Roentgenotherapy of the spleen or splenectomy only increases the anemia, the splenomegaly being a compensatory mechanism. The author believes that the cause is a noxious agent that acts selectively on the recticuloendothelial system.

SWEDEN

Old Age Shift of Pulmonary Tuberculosis.—The general observation that pulmonary tuberculosis has largely become a disease of old age rather than of youth is given statistical support in a study by Dr. Ivar Källqvist in the journal of the Swedish National Association Against Tuberculosis. He has included in his series all the 14,087 patients over the age of 15 admitted to the Söderby Hospital for tuberculosis during the period 1942 to 1954 inclusive. After the elimination of readmissions, the figure was reduced to 12,617. The author then classified the patients according to their age, one group consisting of those under 50 and the other of those over 50. Only 9.6% of the men admitted in 1942 were over 50. After successive rises, the figure reached 31.3% in 1954. Similar figures were obtained for women, with a rise between 1942 and 1954 from 3.3 to 12.2%. Källqvist also studied the age distribution from 1942 to 1954 of all the patients admitted to all the Swedish hospitals for tuberculosis, with the exception of those admitted for surgical tuberculosis. He classified these patients into three groups according to their age: (1) under 15, (2) between 15 and 50, and (3) over 50. He correlated these figures with those referring to the population of Sweden as a whole in the same age group in order to study the tuberculosis morbidity of the country's population at different ages. While there was a fall of the tuberculosis morbidity between 1942 and 1954 in the first two age groups, there was a rise for persons over 50.

Spiritual Welfare of Hospital Patients.—In the fall of 1956 the clergy of Lulea and the medical staff of the Lulea Hospital agreed on the need for more intimate coordination of their respective activities for the benefit of hospital patients. As a result, once every two weeks the two clergymen attached to the hospital take part in the hospital round. They wear the robes distinctive of their calling, and the round is arranged so as to give special opportunities for those patients who might be expected to be in need of spiritual comfort. After one such round a staff meeting was held, and the clergymen discussed the special problems of certain patients. These rounds and staff meetings have enabled the clergymen to become part of the hospital team and to link up the physical with the spiritual ailments of the patients more effectively than in the past. Up to now the clergy have often been in the dark about the somatic ailments of the patients they have visited.

CORRESPONDENCE

CARDIAC SURGERY

To the Editor:—Beck's notable contributions to cardiac surgery put the public and the medical profession greatly in his debt. The figures that he and his colleagues have published are plain for anyone to see and are in no need of the gilding they have received in the article by Brofman in the Dec. 29 issue of THE JOURNAL, page 1603. This paper is so controversial that some comments are necessary regarding a few of the statements that are unintentionally confusing: 1. "By its very nature, this process [coronary artery disease] is progressive and eventually fatal." The reader can only guess at what the author means by the first phrase. The rest of the sentence is contradicted by evidence that is at hand for every clinician and certainly for every pathologist. Any large series of autopsies shows that many old infarcts and coronary atheromas of advanced degree and long standing are discovered in patients who have died of other causes. Many more such lesions, often completely silent, are found by the pathologists than are ever evident clinically. It is much more in accord with the facts to say that a great many people have coronary artery disease and that only a fraction, perhaps half or less, have symptoms or die as a result. 2. "The surgical treatment for coronary artery disease has been established on a firm scientific basis." The author may mean only the Beck 1 operation, although he mentions more than 1,200 operations, done by more than 70 surgeons with an over-all mortality rate between 5 and 10%, without defining the type of surgery used. Whether surgery has indeed a valid scientific basis has troubled many cardiologists, even those, like me, who sometimes advise it. Blumgart and Paul (editorial, *Am. J. Med.* **18**:1 [Jan.] 1955) have recently summarized these misgivings. In any case, most published operations designed for the improvement of coronary disease have fallen into rusty disuse except those, like the Beck 1, which involve the instillation of talc or asbestos into the pericardial sac. 3. "The unreliability of the electrocardiogram was particularly evident in patients in whom serial electrocardiograms had always been normal. In 25% of such patients, exploration of the heart surface . . . revealed previously undiagnosed infarcts." By implication, this would mean that 75% of patients who always had normal cardiographic tracings were found to have normal myocardiums at operation. Should the reader infer that the diagnosis of coronary artery disease was made on the basis of symptoms alone in patients who had no structural defects? 4. "A positive diagnosis of coronary disease is the indication for operation. The achievement of a low operative mortality rate now justifies the application of operation to patients with very early disease . . . ." The meaning of the first sentence is baffling. Does a positive diagnosis mean by symptoms alone as statement (3) would indicate? Does the author mean that the diagnosis of coronary disease alone is the indication? It is quite evident from the fact that 95% of the patients in the series had angina pectoris that the indication for operation was probably the presence of symptoms rather than the mere presence of disease.

This is a point of the most urgent importance, because the reader is left with the impression that the author would like to propose the operation for the sake of prolonging life rather than merely to relieve cardiac pain. If he does indeed mean this, he has very insecure footing. Time may prove that the surgeons are correct; in the meanwhile, the results quoted, considering the difficulties of compiling and evaluating any statistics about coronary disease, seem to be not much better than those obtained in similar cases with medical management (Sigler: *J. A. M. A.* **146**:998 [July 14] 1951).

Medical treatment is making spectacular advances. Newer methods of using glyceryl trinitrate and similar drugs, long-term anticoagulant therapy, and medical ablation of the thyroid gland are improving the lot of the patient with angina pectoris and may be prolonging his life. Even more important, recent (1955 and 1956) investigations of lipid metabolism and dietary management in coronary disease give promise of improving the prognosis and, above all, of correcting one of the fundamental defects causing this disease. On the basis of the best reports so far available, I do not consider it justifiable to recommend operation on the indication of the presence of coronary disease alone with the as yet unproved hope that it may prolong life. Surgery has its place and that is in the treatment of the occasional patient with angina pectoris so intractable that conservative treatment fails.

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HEALTH EXAMINATIONS FOR PHYSICIANS

To the Editor:—In the Jan. 26, 1957, issue of THE JOURNAL, page 304, in the Correspondence section, Dr. Cahall stresses the matter of health examinations of physicians, which was presented on page 1414 of THE JOURNAL of Dec. 8, 1956, by Dr. Lesser. I should like to state that such a program was established in this hospital last fall, and we intend to offer this program to our staff physicians gratis every year. It was interesting to note that, of the first 70 physicians examined, unknown or undetected conditions existed in 15, and these were revealed by the physical examination, laboratory tests, roentgenograms, or rectal examinations. Papanicolaou smears of the cervix were done as part of the examination for females. We believe that, in addition to the value of these yearly examinations, it does build up the morale of the physician in his asso-

ciation with the hospital. We have more than 300 physicians on our staff, and our experience has shown that about 15 examinations could be done at a sitting of about two to three hours. The staff of examining physicians and the hospital offered their services gratis, including x-ray and laboratory tests. I further believe that, inasmuch as the medical profession as a whole recommends annual physical examinations for all people and especially those over 35 to 40 years of age, it is the proper thing for the members of the profession to set the example by having such annual physical examinations themselves.

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POISONOUS FISH

To the Editor:—It is with great interest that I have read the original article "Food Poisoning Caused by the Great Barracuda" by Sidney Paetro, Sanitarian of the Broward County Health Department, Fort Lauderdale, Fla., published in the September, 1956, issue of *Public Health Reports*, page 933, and your editorial in The Journal, Jan. 12, 1957, page 118. As former epidemiologist in Dade County, Miami, Fla., I recall that our department was annually alerted to this problem. This situation has been recurring for years, and much has been studied and written in south Florida concerning the matter of barracuda poisoning. In our experience the clinical picture was typical, as described by all of the investigators. Personal research seemed to indicate that the larger the fish the greater the chance for toxic reactions in the consumer. Many meals including filleted small barracuda were enjoyed by us without any untoward incident. In the opinion of observers and investigators in the area, the toxin appears to be an intraperitoneal agent probably contained in greatest concentration in the bile of the fish and in greater concentration and volume, as would be expected, in the larger specimens. The preparation of the meat by filleting and avoidance of entrance of the peritoneal cavity resulted in a safe food in a relatively small experience. An interesting study could be conducted on animals, with sufficient controls to probably identify the source of the toxin. Afterward, the biochemist possibly could identify the toxin chemically.

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PALATINE PETECHIAE

To the Editor:—It is difficult to know how long a subject should be debated in the columns of The Journal. However, inasmuch as my observations have been mentioned in letters regarding palatine petechiae, perhaps this letter is justified. Despite Warshaw's endeavor (*J. A. M. A.* **163**:143 [Jan. 12] 1957) to "correct the impression" that palatine petechiae can be relied on in diagnosing mononucleosis, the typical lesions, described in the *American Journal of Medicine* (**13**:158, 1952), have continued to prove their reliability to me. I advise continued reliance on these lesions as a most helpful finding in detecting mononucleosis, despite the possibility that they may not be specific. Another writer who has reported on hundreds of personally observed cases of mononucleosis, C. E. Bender, has stated that the palatal enanthem is "very important corroborative evidence" of mononucleosis (*Journal-Lancet* **74**:7, 1954). His article contains a good picture, and verbal description, of the enanthem. In the Army we see many patients with nonspecific, acute pharyngeal inflammations, and many are examined daily; however, my associates and I have not seen the enanthem, as described by Bender and by me, in such cases. Possibly Warshaw has seen lesions of similar, but not identical, appearance. As to priority, as far as I know, Berberich and Thomas were the first to mention this sign, at least in the English-language literature (*U. S. Nav. M. Bull.* **49**:271, 1949).

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WATER FLUORIDATION

To the Editor:—In a pamphlet from California entitled "Fluoridation Unmasked" the following statement about myself appears:

"Professor R. A. Peters, Biochemist of Oxford, England, says: 'Fluoroacetic acid prevents the body from breaking down the citric acid created when sugar is burned into simpler compounds. Retention of waste citric acid acts as a violent poison on heart and nervous system. Fluoroacetic acid is used by African natives to murder their enemies. What will happen to the person drinking fluoridated water when he uses vinegar?' (acetic acid)."

I do not know upon what writing of mine this is supposed to be based, but I think it as well to point out that it gives entirely the wrong impression. Inorganic fluoride acts completely differently in the body from fluoroacetic acid, in which the carbon is linked firmly to the fluorine. Fluoroacetic acid is a rat poison that is much more toxic than fluoride. The suggestion in the last sentence that fluoride and acetic acid will combine easily to form fluoroacetic acid is very wide of the truth. It is in fact quite difficult to synthesize fluoroacetic acid, and certainly there is no evidence that it can happen in the body; furthermore, acetic acid (vinegar), if given early enough, is an antidote to fluoroacetic acid poisoning in some animals.

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ILLUSTRATED FILM REVIEWS

Illustrated reviews of current films will appear when possible as a regular feature in THE JOURNAL. *They will consist of an introduction by the author followed by a pictorial digest of actual frame enlargements selected as key points of the film. It is planned in the future to publish both the illustrated and printed reviews of current films in the same issue.*

Motion Pictures and Medical Television
RALPH P. CREER, *Director*
Council on Scientific Assembly.

RESUSCITATION FOR CARDIAC ARREST

Claude S. Beck, M.D., Cleveland

This film might be called a medical how-to-do-it film, for it outlines and demonstrates a "cardiac resuscitation fire drill."

The film opens with this statement: "Unpredictable cardiac arrest occurs several times each year in every large hospital. This catastrophe may complicate any type of operation . . . every surgeon and every anesthetist can expect to encounter cardiac arrest in the operating room . . . sometime during his professional career."

Scenes showing an actual patient whose heart stopped during local anesthesia for an x-ray procedure remind physicians that prompt action is required when such catastrophes occur.

Then the film shows the prompt purposeful actions—such as quick insertion of the tube into the trachea, the bold opening of the chest, the hand massage of the heart, and the use of drugs and electric shock—that can restart a heart that has stopped for no apparent reason during a surgical procedure.

Next the film repeats the steps of this "cardiac arrest fire drill" on a dog while the medical rationale for each of the steps taken is discussed.

The film concludes with the admonition that the "cardiac resuscitation fire drill" should be carried out at regular intervals in every hospital, for cardiac arrest gives no warning. (This film was reviewed in THE JOURNAL, May 19, 1956, page 272.)

Fig. 1.—"This patient suffered cardiac arrest during local anesthesia for an x-ray procedure."

Fig. 2.—"Dividing the procedure into two steps will help."

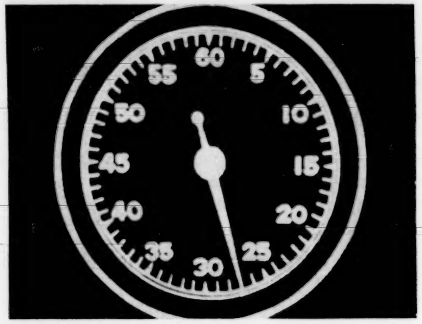

Fig. 3.—"As you well know, the brain without oxygen suffers irreversible damage within three to five minutes."

Fig. 6.—"Inflate and deflate the lungs adequately by compressing a rubber breathing bag filled with oxygen."

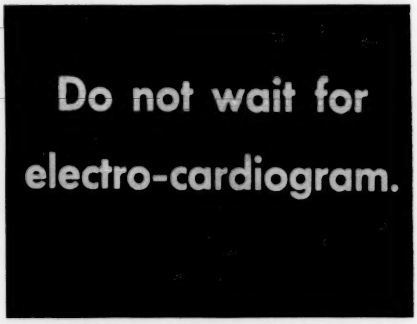

Fig. 4.—"What not to do is just as important as what to do."

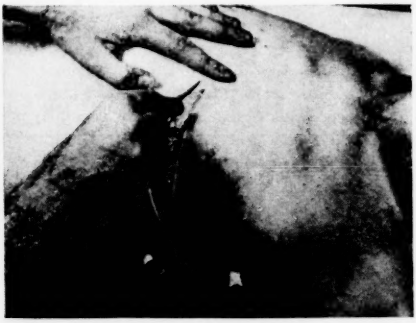

Fig. 7.—"Next, boldly slit open the chest."

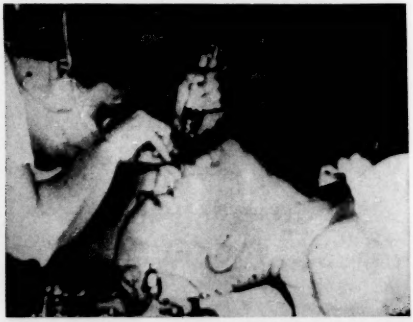

Fig. 5.—"The first thing to do is to get a properly fitting tube into the trachea."

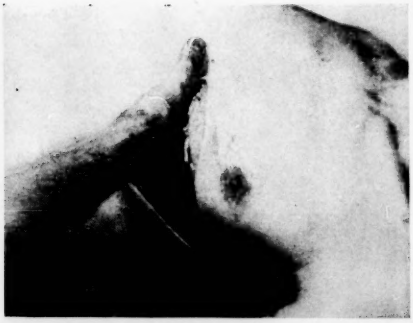

Fig. 8.—"There is no bleeding because there is no blood pressure."

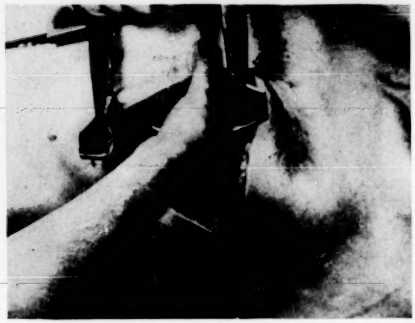

Fig. 9.—"A self-retaining retractor is placed between the ribs to relieve pressure on the surgeon's wrist."

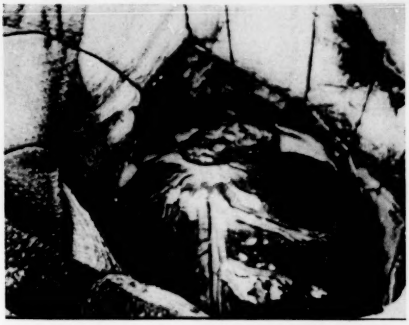

Fig. 12.—"Now, you will see the actual procedure carried out on a dog's heart."

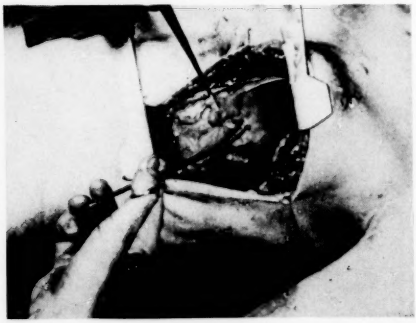

Fig. 10.—"The pericardium is opened from base to apex, avoiding the left phrenic nerve."

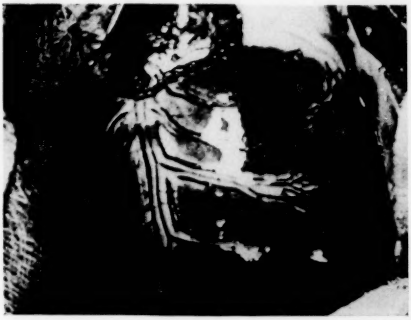

Fig. 13.—"If there's no fibrillary movement, the physician can assume the ventricles are in a state of asystole."

Fig. 11.—"Pumping the heart by hand can maintain adequate blood pressure for hours if necessary."

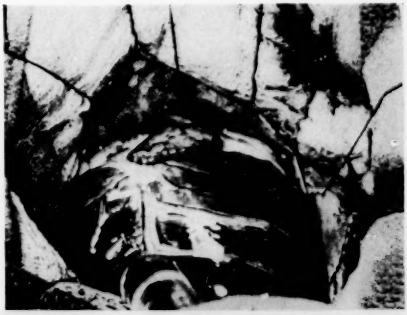

Fig. 14.—"Inject 4 or 5 cc. of diluted 1:10,000 epinephrine solution into the chamber of the right ventricle."

Fig. 15.—"The lungs should come up nicely on inspiration and go down nicely on expiration."

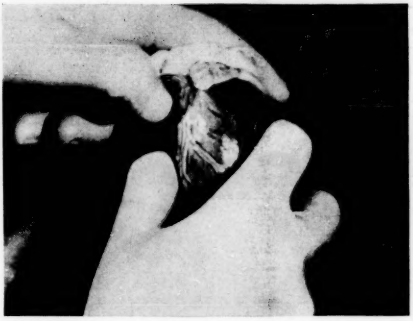

Fig. 18.—"There are several methods of massaging the heart, but the principle behind all methods is the same."

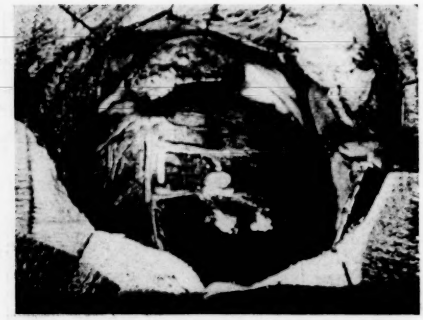

Fig. 16.—"This heart is fibrillating."

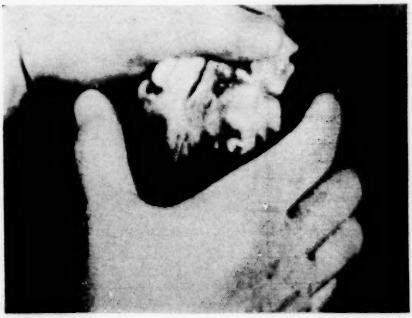

Fig. 19.—"Opening the hand like this must be an active process."

Fig. 17.—"An electric shock is required now."

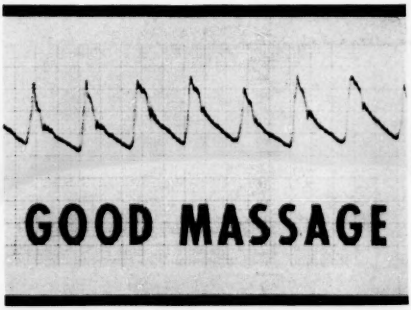

Fig. 20.—"Hand massage can produce a blood pressure high enough to maintain life as long as necessary."

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Treatment of Acute Friedlaender's Bacillus Pneumonia: A Continuing Problem. L. P. Jervey Jr. and M. Hamburger. A. M. A. Arch. Int. Med. **99**:1-7 (Jan.) 1957 [Chicago].

Thirty patients with acute Friedländer's bacillus pneumonia were admitted to the Cincinnati General Hospital from 1939 to 1956. The authors divided this period into two sections, the "prestreptomycin era" and the "era of modern chemotherapy." Streptomycin, tetracycline drugs, or sulfonamides in addition to these were given for the first time in 1948. Prior to that year treatment consisted of sulfonamides only. The mortality of the 15 patients with acute Friedländer's bacillus pneumonia before 1948 was 73%; in the 15 patients treated subsequently it was 53%. Only 2 of 15 bacteremic patients survived. Blood cultures of these patients treated before 1948 were positive in 71%. The incidence fell to 38% in the patients with "modern" treatment. Lung abscesses developed in 7 of the 30 patients. Survivors showed evidence of residual pulmonary disease. It is essential to distinguish Friedländer's pneumonia from pneumococcic pneumonia so that other therapy than with penicillin may be instituted. Sulfonamide treatment seems rather effective. Treatment with streptomycin and tetracycline drugs seems to reduce the mortality still more. The thick tenacious exudate that occurs in Friedländer's pneumonia seems to play an important part in hindering the efficacy of an adequate chemotherapy.

A Long-Term Follow-up of Nontoxic Nodular Goiter: Effect of Clinical Selection on the Observed Incidence of Malignancy. J. E. Sokal. A. M. A. Arch. Int. Med. **99**:60-69 (Jan.) 1957 [Chicago].

An estimated 8,000 patients with nodular goiter were examined at the New Haven Hospital in Connecticut between 1921 and 1945 and were treated conservatively. A 10-year follow-up study was carried out on 296 inpatients in the New Haven hospital listed in the diagnostic index as having nontoxic nodular goiter. One hundred forty of the 296 patients were not operated on within 6 months after the diagnosis of nontoxic nodular goiter had been made; 78 patients received minimal surgical treatment, and another 78 received more extensive surgery including lobectomy, hemithyroidectomy, or bilateral subtotal thyroidectomy. The 140 patients are a 2% sample of the total 8,000 patients who received no surgical therapy. Only 1 of the 140 patients and only a fraction of 1% of the estimated 8,000 patients treated conservatively had thyroid cancer at the time the original decision regarding therapy was made, and thyroid cancer did not occur in these patients since then. The excised nodule proved to be malignant on microscopic examination in 2 of the 78 patients who underwent minimal surgical treatment (prophylactic adenomectomy), and cancer did not develop after the adenomectomy in any of the remaining 76 patients. Thirteen (16%) of the 78 patients who underwent lobectomy, hemithyroidectomy, or bilateral subtotal thyroidectomy had malignant goiter. These figures demonstrate impressively the efficiency of preoperative selection in nontoxic nodular goiter.

The follow-up study of the 296 patients represents 3,000 patient-years of observation of persons with nontoxic nodular goiter. No new thyroid cancers have become evident during this time. This confirms previous estimates that the incidence of malignancy in this condition is quite low. Conservative management of selected patients with nontoxic nodular goiter is justified.

An Intrafamilial Epidemic of Pharyngoconjunctival Fever. R. G. Van Horne, S. Saslaw, G. R. Anderson and others. A. M. A. Arch. Int. Med. **99**:70-73 (Jan.) 1957 [Chicago].

The authors report on an epidemic of pharyngoconjunctival fever that occurred in 6 of the 7 members of a family consisting of the parents and 5 children between the ages of 1 and 14 years. The clinical findings of fever, pharyngitis, conjunctivitis, rhinitis, malaise, and cervical adenitis were associated with successful APC type 3 virus isolations and significant elevations of specific serologic titers in 3 children. No virus was recovered from the youngest child, who was well again at the time he was examined first, but he had the typical clinical history of pharyngoconjunctival fever. A 2-year-old boy was the only child in the family who did not become ill and showed correlative negative virus studies. The parents had pharyngitis and mild fever but did not have conjunctivitis. They failed to yield virus in culture and showed no significant serologic titers.

All patients responded to supportive therapy alone. The incubation period was apparently between 5 and 8 days as the disease progressed through the family. The virus was isolated only from the 3 acutely ill persons, from the conjunctiva, pharynx, and stool. No virus isolation could be accomplished one month after the patients' recovery. The complement-fixation titers,

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The place of publication of the periodicals appears in brackets preceding each abstract.

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which are group-specific, and the type-specific neutralization titers both rose in the 3 patients with positive cultures during the acute phase of the illness. Complement-fixing antibodies could not be demonstrated in any member of the family after 7 months, although the neutralization titers remained elevated. These data suggest that the complement-fixation titer is transient in nature, while the neutralization titer is more persistent.

Pseudohypoparathyroidism. J. V. Cusmano, D. H. Baker and N. Finby. Radiology **67**:845-853 (Dec.) 1956 [Syracuse, N. Y.].

Hypoparathyroidism is most commonly seen following thyroidectomy, after inadvertent or unavoidable removal of the parathyroid glands. Spontaneous or idiopathic hypoparathyroidism is rare. Albright recognized the occurrence of 2 forms of the latter condition when he found that in some cases the patient failed to respond to large doses of parathormone. It is these cases that are designated pseudohypoparathyroidism. The authors present the histories of 6 patients with pseudohypoparathyroidism, 2 of whom were twin sisters. The ages of the 6 patients ranged from 5½ to 29 years. Thirty cases have been reported in the literature. The symptoms of the disease are due chiefly to episodes of hypocalcemia. Tetany, with manifestations of stridor, muscular hyperexcitability, tonic convulsions, tingling, and cramps of the extremities, is seen at some time in every patient with this disease. Other significant findings are mental retardation, delayed and defective dentition, cataract formation, and the characteristic round face and short, stocky appearance. Older persons may show immobile facies and posture suggestive of paralysis agitans. There is evidence that pseudohypoparathyroidism is a familial disease with 3 components: first, the metabolic defect, which is manifested as a failure to respond to parathormone; second, bone dysplasia; and third, extraskeletal calcification and ossification. The roentgenographic findings of short metacarpals, thickened calvarium, and extraskeletal calcifications, singly or in combination, in patients with symptoms of parathyroid insufficiency, should suggest the diagnosis of pseudohypoparathyroidism.

Corticotrophin and Cortisone Therapy in Dermatomyositis. M. McElligott. Brit. M. J. **2**:1509-1511 (Dec. 29) 1956 [London].

Three women between the ages of 30 and 49 years with dermatomyositis were treated with corticotropin gel at the Newcastle General Hospital in England. The first patient had an extremely acute toxic attack, for which 60 mg. of the drug was given every 12 hours. A response occurred within 12 hours, with temperature of 105 F (40.6 C) being restored to normal and drop of pulse rate from 120 to 90 per minute. The patient felt well after 30 days of treatment with corticotropin; muscle contractures were absent, but some wasting was still evident. There was brown pigmentation on the face, upper limbs, and trunk. Transient hypopotassemia was treated by administration of potassium chloride. The dose of corticotropin was reduced gradually by 5 mg. daily, and the drug was withdrawn after a total dose of about 5 gm. had been administered. A follow-up examination 9 months later revealed complete recovery and a gradual resolution of the Cushing-like character of the face. The second patient received a total dose of 2.2 gm. of corticotropin in the course of 34 days, and the initial dose of 60 units of corticotropin twice daily was reduced gradually after 7 days. Recovery was complete except for some paralysis and wasting of the small muscles of the left hand, which resolved on physical therapy over a period of several months. Nine months later the patient had gained weight and was symptom-free. The third patient differed from the 2 others by the less elevated temperature (100 F [37.8 C]), absence of leukocytosis, positive muscle biopsy, gross muscular weakness, and marked muscle edema. The case was one of "chronic dermatomyositis." She showed instantaneous improvement when 60 mg. of corticotropin gel was given every 12 hours, although the muscles, with the exception of those of the arms, remained unchanged. Transient dysphagia and concomitant paralysis of the soft palate occurred on the 8th day of treatment, and the dose of the drug was increased to 80 mg. given intravenously over a period of 12 hours. There was no improvement, and the patient's condition was deteriorating rapidly. Corticotropin was withdrawn and the patient was given 75 mg. of cortisone every 12 hours, but death occurred 48 hours later. The patient had received a total dose of 1.44 gm. of corticotropin and 300 mg. of cortisone.

The observations in the 3 patients and in those reported by other workers suggest that cortisone or corticotropin can be a life-saving drug in patients with an acute fulminating attack of dermatomyositis, and the effect of the drug is dramatic. The drug usually fails to improve the more chronic form of the disease, but it should never be withheld because of the occasional success claimed in patients of this type. A curative effect of corticotropin and cortisone on dermatomyositis associated with neoplasm has been likewise described.

Hazards in the Use of Anticholinergic Drugs in the Management of Peptic Ulcer Disease. J. L. A. Roth, R. L. Wechsler and H. L. Bockus. Gastroenterology **31**:493-499 (Nov.) 1956 [Baltimore].

Complications may arise during the prolonged use of methantheline bromide (Bantine) in patients with peptic ulcer. The authors report on 3 patients out of 12 with similar situations during a 3-year experience. Methantheline appeared to have reduced the severity of the ulcer distress. The mildness of symptoms gave the patient a false sense of security regarding the healing of his ulcer. X-ray examinations showed persistence of the ulcer crater despite administration of methantheline for 7 months. Resection of the stomach and a complementary vagotomy were performed. Pain, which served as a warning of ulcer recurrence and bleeding, was so altered in another patient that he failed to recognize the severity of his disease. Perforation occurred, although methantheline had been used for several months. Surgical intervention was neces-

sary. A 3rd patient abandoned conventional ulcer therapy when the pain was minimized by methantheline. X-ray examination showed the persistence of the ulcer crater, despite many months of methantheline therapy. Methantheline may be used as an addition to the conventional "physiological stomach rest" regimen in the treatment of uncomplicated peptic ulcer. Its use in the "prophylaxis of peptic ulcer" is to be avoided. Methantheline therapy should at any time be accompanied by a control of the possible masking of recurrences and/or complications.

Acquired Hemolytic Anemia Caused by Ingestion of Fava Beans: Report of a Case and Review of Cases Reported in American Literature. W. R. McPhee. Am. J. Clin. Path. **26**:1287-1302 (Nov.) 1956 [Baltimore].

McPhee reports a case of favism in a 4-year-old boy of Italian extraction who was admitted to hospital with malaise, fever, hematuria for 2 days, and jaundice for 1 day. He had eaten fava beans raw 3 days before and cooked 2 days before admission. He was given 500 cc. of whole blood in the afternoon of the 2nd day in the hospital, and he received an additional 250 cc. the following morning. Improvement began on the evening of the 2nd day in the hospital and continued. He was discharged 5 days after admission. Fifteen additional cases of favism were collected from the literature in the United States. Thirteen of the 15 patients were males, 11 were of Italian descent, 10 were aged 5 years or less. The illness generally began suddenly with anorexia, weakness, pain in the abdomen, and malaise. Nausea and vomiting, chills and fever, and diarrhea occurred frequently. Hemoglobinuria was observed in 12 and jaundice in 13. History revealed ingestion of fava beans in all the patients. There were no deaths. Laboratory studies revealed a proportionate decrease in the red blood cell count and in the level of hemoglobin. Most of the people who cultivate and eat fava beans in the United States are of Italian extraction. The fresh, green beans or the pollen are thought to be responsible for most of the severe cases of favism. Hypogammaglobulinemia may prove to be the most significant factor in the development of the acute hemolytic anemia that results from sensitivity to fava beans or the pollen of the flowering plant.

Fungal Diseases in a General Hospital: A Study of 88 Patients. J. D. Keye Jr. and W. E. Magee. Am. J. Clin. Path. **26**:1235-1253 (Nov.) 1956 [Baltimore].

A study of the clinical records and the autopsy findings of 15,845 patients at Barnes Hospital in St. Louis on whom autopsies were performed between 1919 and June, 1955, revealed 88 patients with fungal infections. Twenty (23%) of the 88 patients had histoplasmosis, 13 (15%) cryptococcosis, 9 (10%) mucormycosis, 25 (28%) candidiasis, 3 (3.5%) aspergillosis, 9 (10%) actinomycosis, 7 (8%) blastomycosis, and 2 (2%) coccidioidomycosis. The fungus disease was primary in 41 of the 88 patients and secondary in 47. The incidence of primary fungal infections did not change since 1947 when treatment with multiple antibiotics began, but there was a striking increase in the incidence of secondary fungal infections. Histoplasmosis, cryptococcosis, mucormycosis, candidiasis, and aspergillosis accounted for this increased incidence. Forty of the 47 patients with secondary fungal infections were observed since 1942, when treatment with penicillin began. Thirty of these 40 patients were treated for their primary disease with antibiotics for at least 7 days, and 21 of them had leukemia or malignant lymphoma.

These data suggest a tendency for more extensive and widespread dissemination of fungal infections in recent years, as compared with that observed before the use of antibiotics. This particularly applies to secondary fungal infections in patients with leukemia or lymphoma. Extreme variability was noted in the extent and significance of fungal infections, particularly those caused by Candida albicans. The secondary fungal infections were commonly associated with infections by antibiotic-resistant bacteria, particularly micrococci (staphylococci). Clinical diagnosis of secondary fungal infections is difficult, and a high index of suspicion is required if such infections are to be recognized clinically. The sharp rise in the incidence of fungal infections since 1947 is believed to be definitely related to therapy. Multiple antibiotics; chemotherapeutic compounds such as nitrogen mustard, triethylene melamine, antagonists of folic acid, 6-mercaptopurine, and busulfan (Myleran) used in the treatment of leukemia and lymphomas; and cortisone were the therapeutic agents most frequently administered to patients with secondary fungal infections. Evaluation of the effects of therapy as precipitating factors in the development of secondary fungal infections is difficult because of the presence of a serious, underlying disease and the diversification of therapy.

Anaphylactoid Reaction to Penicillins V and G Administered Orally. Report of Two Cases and Brief Review of the Subject. H. C. Maganzini. New England J. Med. **256**:52-56 (Jan. 10) 1957 [Boston].

The author reports the histories of 2 patients in whom an anaphylactic reaction resulted from the oral administration of penicillin. These 2 cases were encountered 24 days apart in the emergency room of a 192-bed hospital. In 1 patient the reaction was due to penicillin V (phenoxymethyl penicillin), and the other patient had a nearly fatal reaction to penicillin G. Reviewing the available literature on reactions to orally administered penicillin, the authors found that, with the addition of these 2 cases, a total of 13 due to tablets are on record, and in addition lozenges caused 12 reactions. Penicillin V is not hypoallergenic and should not be given to susceptible persons, especially not to those with any previous reaction to other forms of penicillin. Positive skin and passive-transfer tests demonstrate marked sensitivity and contraindicate the use of penicillin, but negative tests do not rule out anaphylactic reactions. A patient who is to receive penicillin by any route should be questioned concerning previous penicillin administration and possible reactions, atopy, and asthma. Penicillin reactions are increasing, and with the more widespread use of

preparations for oral use all physicians should be familiar with and able to cope with the immediate anaphylactic reaction. Anaphylaxis should be considered in the differential diagnosis of shock of obscure origin. A careful examination should be made for the presence of minor degrees of lip or periorbital edema and minimal skin lesions.

SURGERY

The Treatment of Cancer of the Breast. J. C. Smith. Surg. Gynec. & Obst. **104**:36-40 (Jan.) 1957 [Chicago].

The principle of treatment of cancer of the breast is the eradication of all tumor cells from the largest amount of tissue at the earliest moment with the least risk. Simple mastectomy clears too little tissue of all tumor cells and is an inadequate method of therapy. Ultraradical mastectomy offers little benefit over the accomplishment of the standard radical procedure and entails a higher risk of operative complications. The rate of survival expresses the ratio of tumor-cell distribution to the amount of tissue cleared of tumor. It is determined principally by the variable of tumor-cell distribution and, therefore, survival rates are unreliable expressions of therapeutic accomplishment. The rate of survival discloses the proportion of cases in which all tumor cells lay within the tissue encompassed by the method of treatment. Progressively favorable rates of survival after the same method of treatment reflect higher proportions of cases treated while all tumor cells are circumscribed about the primary site. Such results may be credited to the programs of cancer education that emphasize early detection and the importance of the time factor in the curability of cancer. Progress in the treatment of cancer of the breast depends on increasingly early detection, prompt application of the superior method of treatment, and selection of that method according to compliance with the principle of treatment rather than by a comparison of survival rates.

Acute Pancreatitis Following Subtotal Gastrectomy. H. E. Haffner and E. G. Ramsay. Missouri Med. **54**: 29-33 (Jan.) 1957 [St. Louis].

Pancreatitis developed postoperatively in 4 of 176 patients who underwent subtotal gastrectomy for duodenal ulcer, and 2 of the patients died. The treatment of acute pancreatic disease occurring postoperatively is essentially the same as that for primary pancreatitis. Symptomatic treatment is required for shock, pain, infection, and pleural effusion. The mainstays of treatment are antibiotics, continuous gastric suction, oxygen therapy, intravenous fluids, electrolytes, whole blood, calcium, meperidine for pain, and, in some cases paravertebral procaine block or epidural anesthesia. If acute diabetes occurs, it requires the judicious use of insulin. Surgical procedures are generally of no help and may be detrimental. The development of an abscess requires drainage. In view of recent work on adrenal cortical exhaustion during and after major surgery, intravenous administration of hydrocortisone may be of benefit.

Adrenalectomy in Advanced Malignant Tumors. G. M. Miller. Rocky Mountain M. J. **54**:34-38 (Jan.) 1957 [Denver].

The author comments on the rationale for bilateral adrenalectomy in hormone-disseminated cancers of the breast and prostate and tabulates the results obtained with this operation in 5 reported series, which comprised a total of 228 women with breast cancer who underwent bilateral adrenalectomy and oophorectomy. Subjective improvements include relief of intractable pain, disappearance of respiratory symptoms, return of a sense of well-being, and increase in appetite, weight strength, and vitality. Objective improvements include disappearance of local and of metastatic pleural and pulmonary lesions, involution of lymph node lesions, improvement in the level of alkaline phosphatese, and healing of cancerous ulcers, of pathological fractures, and of osteolytic defects. Subjective improvement was observed in from 45 to 60% of the 5 series of patients and objective improvement in from 22 to 40%. These percentages of beneficial results indicate that these surgical procedures offer an important and useful additional therapeutic tool in the treatment of advanced mammary cancer. Results in a much smaller collected series of patients with disseminated prostatic cancer indicate that bilateral adrenalectomy is not as effective in this disease. It does not appear to be a practical tool for cancer of the prostate, and large doses of cortisone should be used first.

Results of Treatment of Carcinoma of the Breast in General Surgical Practice. K. E. Lister, G. C. Blome, E. B. Howell and H. L. Wormhoudt. J. Iowa M. Soc. **47**:20-23 (Jan.) 1957 [Des Moines].

Lister and associates performed 165 radical mastectomies for carcinoma of the breast over a 15-year period. Ninety-eight patients were operated on more than 5 years ago, and all but 2 of these were followed-up either to the present time or until they died. Fifty-nine of the 98 patients had stage 1 lesions, and of these, 49, or 83.4%, survived 5 years or more, whereas of the 39 who had stage 2, 3, or 4 lesions, only 16, or 41%, survived 5 years. The over-all 5-year survival rate was 65%, but nearly 60% of these women had stage 1 lesions. Of 28 women who survived more than 5 years after operation for stage 1 lesions, 20 survived 10 years, and 6 of the 8 patients who died during the second 5-year term died of metastases. Of 16 women who had been operated on for lesions more advanced than stage 1, only 4 survived 10 years. This shows that it is a fallacy to equate 5-year survivals with clinical cure.

Cytological activity and anatomic extent are of prognostic importance. The breast and axillary structures are removed "en bloc" from the chest wall. Postoperatively, they use negative-suction catheters beneath the flaps to the exclusion of pressure dressings and feel that by doing so they have reduced the morbidity of wound closure. Suction is used until the daily accumulation of serum is 40 cc. or less. The catheters are then removed, and the dressing is maintained without pressure. For the past 2 years, they have performed the

more radical resection for medial and subareolar lesions that has been advocated by Wangensteen and others. It consists of the resection of the medial ends of the 2nd, 3rd, and 4th ribs, along with the internal mammary vessels and nodes. Perhaps 30 to 45 minutes are thus added to the operating time, but the cure rate of lesions in the medial half can thus be increased by as much as 15%. The lengthening of the procedure does not add to its morbidity or mortality, but it does necessitate the use of intratracheal anesthesia and suction beneath the flaps to permit adequate reexpansion of the lung. The authors believe that preoperative irradiation is of no value and that castration should be limited to premenopausal women having stage 2, 3, or 4 lesions. There is evidence that results achieved in the treatment of carcinoma of the breast in a small medical center can compare favorably with those secured at larger institutions.

The Surgical Treatment of Hypertension: Discussion of Its Applications. G. Favacchio and A. Pesci. Policlinico (sez. prat.) 63:1521-1528 (Oct. 22) 1956 (In Italian) [Rome].

The results obtained in 29 patients with hypertension who were subjected to sympathectomy are reported. In most patients the 11th rib is resected, the splanchnic nerves are identified and resected, and the celiac ganglion and the aorticorenal ganglion are also removed. This technique has a low fatality rate, permits a complete denervation, does not cause undesirable side-effects, and, when indicated, gives good results. Far better results are obtained with a bilateral resection of the splanchnic nerves and of the ganglionic chain. The operation is contraindicated in patients over 50 and in those with renal insufficiency. Cardiac deficiency and recent infarction are serious contraindications when associated with renal deficiency or with severe alterations in the eyegrounds. Cerebral lesions constitute serious contraindications if combined with poor heart condition, severe alterations in the eyegrounds, or diastolic pressure above 140 mm. Hg. The operation is indicated for patients in fair general condition who are below 45 years of age, who have a diastolic pressure below 140 mm. Hg, and who do not have irreversible cardiac, renal, or cerebral lesions. In general, the operation is more frequently indicated for women than for men.

The Value of Lumbar Sympathectomy in Intermittent Claudication. J. C. Luke. Surgery 41:165-171 (Jan.) 1956 [St. Louis].

Pain in the foot, calf, thigh, buttock, or low back that comes on when walking and is relieved by a short rest is typical of true claudication due to obliterative arterial disease. Pain felt in the foot usually means main vessel occlusion below the knee; if in the calf the occlusion is usually in the popliteal or femoral arteries or higher; in the thigh the iliac arteries are involved; and in the low back and buttocks lower aortic occlusion is usually the cause. This diagnostic impression can be confirmed by the clinical examination with determination of the existing palpable pulses and the oscillometric readings. Aortic or femoral arteriograms will give a visual presentation. It should be remembered that intermittent claudication (usually calf) can resolve spontaneously. The author has at least 10 patients who, when seen initially with calf claudication, showed no palpable pulses below the common femoral and low calf oscillometric readings. In 6 to 8 months the claudication had disappeared and the oscillometric readings had improved. Most of these recoveries were spontaneous with no treatment. If such a patient had been under any form of therapy, including use of vasodilator drugs or lumbar sympathectomy, an erroneous opinion of the efficacy of this treatment would have been formed. The explanation seems to be that a segmental occlusion was bypassed by a collateral circulation.

Seventeen patients are presented in whom arteriography revealed that an occlusion existed in the popliteal artery. Calf claudication was the only symptom in all these patients, who were men ranging in age from 42 to 67 years. These patients were subjected to lumbar sympathectomy, with improvement in walking distance of threefold or more. Because of the results obtained in these patients, the author feels that patients with popliteal artery occlusion can be promised such improvement if the 1st, 2nd, and 3rd lumbar ganglions are removed. This is in contrast to little or no improvement in walking distance when sympathectomy is performed in patients with claudication whose level of occlusion is higher in the femoral artery. The collateral circulation about the knee is the probable factor in the difference in results between the popliteal and femoral levels.

Critical Analysis of Palliation Produced by Adrenalectomy in Metastatic Cancer of the Female Breast. C. P. Perlia, S. Kofman, D. Nagamani and S. G. Taylor III. Ann. Int. Med. 45:989-1000 (Dec.) 1956 [Lancaster, Pa.].

Fifty-eight female patients with metastatic carcinoma of the breast underwent bilateral adrenalectomy in the steroid tumor clinic of the University of Illinois and the Presbyterian Hospital between February, 1952, and August, 1955. Histological diagnosis of the primary tumor was available for all cases. Definite evidence of recurrent metastatic disease was obtained for every case, either by biopsy of accessible lesions, cytology of effusions, or by analysis of roentgenograms. All but 2 patients had received previous standard therapy for metastatic disease, and all showed progression of their disease at the time adrenalectomy was performed. Serial roentgenograms, chest and bone surveys, and serum calcium and alkaline phosphatase and urinary calcium excretion studies were obtained at intervals of 4 to 6 weeks, and the results were correlated with the clinical picture.

Eight of the 58 patients died within the immediate postoperative period; extensive pleuropulmonary involvement was the cause of death in 5. Two died from hepatic insufficiency secondary to metastatic disease and 1 from postoperative hemorrhage. In the remaining 50 patients, worthwhile palliation was obtained in

13, or 26%. Three more patients demonstrated objective regression, but palliation did not take place. No correlation could be demonstrated between previous response to various therapies and the results following adrenalectomy. The evaluation of objective regression of metastatic breast tumor is difficult, and conclusions may be fraught with errors. Further evaluation of a large pooled series of cases is necesary before the validity of the procedure can be established.

Thoracolumbar Sympathectomy for the Treatment of Hypertension: Functional and Anatomosurgical Foundations of the Technique of E. Malan. A. Puglionisi. Minerva cardioangiol. 4:595-606 (October) 1956 (In Italian) [Turin, Italy].

Sympathectomy according to a technique developed by E. Malan was performed on 15 patients with hypertension. The results were superior to those obtained in sympathectomies performed according to the Smithwick technique, which had been used in the clinic of the author from 1948 until 2 years ago. The Malan technique permits the resection of the sympathetic ganglion chain from the 5th thoracic ganglion to the 2nd lumbar ganglion inclusive and the removal of the 3 abdominal splanchnic nerves. The author made a study on 11 cadavers to find out the number and the position of the original branches of the greater splanchnic nerve and to find out how far the sympathetic chain should be resected in order to secure a complete removal of the nerve. The author studied also the presence of other accessory splanchnic branches that take origin in the upper thoracic ganglions and at times connect with the celiac plexus; if these accessory branches are not resected, the splanchnic denervation results are incomplete. Four original branches of the splanchnic nerve were found in 1 cadaver, and they originated in the 5th to the 8th ganglion of the sympathetic ganglion chain; in another cadaver there were 4 original branches that originated in the 6th to the 8th ganglion; in 5 cadavers there were 3 original branches that originated in the 6th to the 8th ganglion; in 1 cadaver there were 5 original branches that originated in the 6th to the 9th ganglion; in 2 cadavers there were 4 original branches that originated in the 6th to the 9th ganglion; and in the last cadaver there were 3 original branches that originated in the 7th to the 9th ganglion. The author concludes that in order to remove the upper root of the splanchnic nerve it is necessary to make a denervation as far up as the 5th thoracic vertebra.

Indications for Surgical Treatment of the Postphlebitic Syndrome. J. C. Owens and L. L. Anderson. Surgery 41:81-93 (Jan.) 1957 [St. Louis].

During the 4-year period since 1952, a total of 154 patients in the indigent or low-income groups were treated. Although the period of observation of some patients is short (minimum 6 months), the majority were observed long enough to permit certain conclusions. The diagnosis of the postphlebitic syndrome in the 154 patients was based on a history of deep vein thrombophlebitis followed by edema and any combination of skin pigmentation, dermatitis, subcutaneous fibrosis, chronic ulceration, varicose veins, recurrent infection, and such disabling subjective symptoms as heaviness, fatigue, and pain. In some patients without history of thrombophlebitis, the typical findings of the syndrome were present, but no other known cause (e. g., cardiac disease, primary lymphatic obstruction, simple varicose veins) could be found; these were considered nonthrombotic. This group numbered 23, while 129 patients showed classical evidence or had a history placing them in the thrombotic group.

Conservative treatment produced satisfactory results in 85% of the 154 patients. The program requires education of the patient and his complete cooperation, also vigorous treatment of allied disorders, control of local infection, and elevation, compression, and exercise followed by progressive edema-free ambulation with compression. Unsatisfactory results occur when the patient fails to meet this program. Indications for surgery have been few with this regimen. The authors operated upon only 27 of the 154 patients. Reasons for operation were an occasional graft for indolent ulcer that failed to heal within a 3-to-4-month period, especially if malignancy was suspected, because of its appearance or extremely long duration; or brawny, indurated legs with or without large unresponsive ulcers, in which the edema did not subside in 1 month. Excision of varicose veins, the most common operation in this series, was done for symptomatic relief only when the postphlebitic edema had been controlled for a significant period. Surgery has its place but should be reserved for those complications that have failed to clear after a thorough conservative regimen.

NEUROLOGY & PSYCHIATRY

Permanent Relief of Tic Douloureux by Gasserian Injection of Hot Water. R. Jaeger. A. M. A. Arch. Neurol. & Psychiat. 77:1-7 (Jan.) 1957 [Chicago].

One hundred patients with typical tic douloureux (major trigeminal tic) were given injections of boiling water into the Gasserian ganglion with the aid of very light thiopental (Pentothal) sodium anesthesia. With a "twilight-sleep" depth of anesthesia, the extent and degree of analgesia or hypalgesia can be determined precisely during the injection by the involuntary muscle responses of the patient's face and feet to pinprick over the painful area. Insufficient hypalgesia or anesthesia over the affected part of the face may require repeating the injection or increasing the amount of boiling water. A short beveled 3¾-in. 17-gauge or 18-gauge spinal needle is inserted through the cheek below the malar bone and medial to the ramus of the lower jaw, making certain by direct intraoral inspection that the needle has not punctured the mucous membrane and contaminated the needle point. It is pointed to a location anterior to the foramen ovale at the base of the skull, where its tip is precisely located by the x-ray on Polaroid or conventional film taken from below the mandible on a line perpendicular to the base of the skull. When the foraminal opening is visualized and palpated, the needle is advanced 1

cm. through it, where it will lie very near or among the ganglion cells. Some 2 cc. of boiling water may be required at a single injection to produce the desired result. Slightly larger amounts of water will usually be necessary if the fluid-bearing subarachnoid space around the ganglion has not been entered, but more than 2.5 cc. at a single injection was considered unwise for fear of causing a temporary paresis of the extraocular nerves. In the event of a failure it is better to wait for 2 days and then repeat the procedure.

Ninety-three patients obtained complete relief of sharp tic pains and 3 obtained partial but satisfactory relief. Two, with inadequate facial hypalgesia, had a late return of pain which was stopped by a second injection. Four were therapeutic failures. Facial paralysis or weakness, corneal ulcer, or corneal complications did not occur in any of the patients. Facial herpes was observed in 3, extraocular weakness lasting from 3 to 5 months in 5, and severe postinjection paresthesia in 4. The method is as permanent a cure for tic douloureux as is available at present. Another injection can be performed with no greater risk or pain than the first, should the pain extend to other parts of the face not formerly affected. The advantage of the author's method appears to be the avoidance of a major brain operation with attendant shock, low mortality, permanence, absence of serious eye complications, no facial paralysis, and painlessness. The procedure requires knowledge and experience of a neurosurgeon for safe and satisfactory results.

Recent Concepts of the Pathogenesis of Poliomyelitis. G. Kersting, H. Lennartz and H. Pette. München. med. Wchnschr. **98**:1684-1688 (Dec. 7) 1956 (In German) [Munich, Germany].

After reviewing 4 concepts of the dissemination of the poliomyelitis virus within the organism, the authors report the results of their experiments with animals on the pathogenesis of poliomyelitis. They resorted to various modes of virus inoculation in different species of monkeys. After all methods of virus administration, including the oral one, virus could always be detected in the cerebrospinal fluid in close chronological relation to viremia and to the onset of paralysis, and the authors believe that this supports the concept of the direct hematogenous invasion of the central nervous system by the poliomyelitis virus. This pathogenetic concept, which is one of the foundations of Salk's vaccination with inactivated poliomyelitis virus, is not quite compatible with the observation that this form of vaccination prevents most of the paralytic cases but apparently only a small portion of the nonparalytic cases of poliomyelitis.

In commenting on possible reasons for this, the authors also mention the view of Sabin, who inclines to Verlinde's concept of pathogenesis and believes that this explains the lack of protection by Salk's vaccine against the nonparalytic forms of poliomyelitis. Since, according to this concept, the antibodies that form after vaccination can neutralize only a part of the invading virus particles, only the severe forms of the disease are rendered less severe. Sabin presupposes that the severity of the lesion of the central nervous system depends directly on the quantity of virus reaching the nervous system. This, however, does not agree with the results of virus titration in experiments with animals, in which the use of greater dilutions (more attenuated) is always followed by a reduction in the number of infections, not by a lessening of the severity of the clinical findings.

Cerebral Manifestations of Vitamin-B_{12} Deficiency. J. M. Holmes. Brit. M. J. **2**: 1394-1398 (Dec. 15) 1956 [London].

Holmes observed 25 patients with changes in the nervous system, including the spinal cord, peripheral nerves, and brain, caused by vitamin B_{12} deficiency. The term neurological syndrome of vitamin B_{12} deficiency would be more satisfactory than the previously applied term of subacute combined degeneration. Fourteen of the 25 patients between the ages of 32 and 72 years with hemoglobin levels ranging from 32% to 105% had well-marked cerebral symptoms and were studied in detail. The cerebral symptoms were mental and ophthalmologic. The mental symptoms were extremely variable and included mild disorders of mood, mental slowness, memory defect, confusion, depression of varying degree, delusions, visual or auditory hallucinations, dysphasia, extreme agitation, violent manic behaviour, and epilepsy. The ocular disturbances consisted of dimness of vision caused by optic atrophy. The diagnosis was established in these patients by the presence of signs of spinal involvement or peripheral neuropathy, evidence of pernicious anemia in the blood cell count or bone marrow, and the presence of a histamine-fast achlorhydria in the gastric juice, which was a feature in each of the 14 patients. The cerebral symptoms preceded the appearance of pernicious anemia or of spinal and peripheral nerve involvement by several years in some patients. Good recovery from the varying degrees of mental derangement occurred in 11 patients after intensive treatment with cyanocobalamin. An initial dose of 1,000 mcg. followed by 500 mcg. twice weekly for the first month and thereafter not less than 100 mcg. weekly for the next 6 months proved to be effective.

Two of the patients died, and autopsy was performed in 1. The findings in this patient and those that were supplied in another case in which autopsy was performed elsewhere, confirmed that the lesions in the brain of patients with established vitamin B_{12} deficiency and psychotic symptoms are essentially similar to those observed in the spinal cord in subacute combined degeneration and consist of diffuse and focal areas of degeneration in the cerebral white matter, with relatively little proliferation of fibrous glia.

The evidence that the cerebral symptoms observed in the patients are specifically related to the vitamin B_{12} deficiency and not to anemia is discussed by reference to recent literature. The diagnosis is also discussed, and the lack of correlation between the hematological and neurological manifestations and between the spinal and cerebral symptoms of the syndrome is considered the great difficulty in establishing the diagnosis of vitamin B_{12} deficiency with in-

volvement of the nervous system. Early diagnosis is essential if treatment is to be effective, for the reversibility of neurological symptoms is largely dependent on their duration. Recently developed techniques, such as the assay of vitamin B_{12} in the serum using the specific effect of vitamin B_{12} on the growth of the alga Euglena gracilis, gastric biopsy, and electroencephalography, may be valuable in patients in whom there is no evidence of macrocytic anemia, megaloblastic reaction in the bone marrow, or subacute combined degeneration of the cord.

Poliomyelitis and Prophylactic Inoculation Against Diphtheria, Whooping Cough, and Smallpox: Report of the Medical Research Council Committee on Inoculation Procedures and Neurological Lesions. Lancet 2:1223-1231 (Dec. 15) 1956 [London].

From 1950 on, there were reports that there was occasionally a causal relation between paralytic poliomyelitis and the inoculation of prophylactics against diphtheria and whooping cough. Children with paralytic poliomyelitis who had had an injection of diphtheria or whooping-cough prophylactic or smallpox were investigated, and 355 paralytic cases were studied. Paralysis developed from 1 to 28 days after inoculation in 132 of 222 children with poliomyelitis who had completed a primary course of inoculations or had been given reinforcing doses. These cases were concentrated around the 11th and 17th days after inoculation. It was estimated that about 1 in 37,000 inoculations precipitated paralytic poliomyelitis. There was evidence that the risk did not extend beyond 1 month after the inoculation and that a series of inoculations had no cumulative effect. The risk varied with the nature of the prophylactic used, being greatest with alum-precipitated diphtheria-pertussis vaccines; mixed nonalum precipitated prophylactics occupied an intermediate position, and plain pertussis vaccine appeared relatively safe. There was no evidence of a provoking effect due to smallpox vaccine.

It was estimated that about 13% of paralytic cases of poliomyelitis in children 6 months to 2 years of age in the county boroughs and large urban areas were causally related to inoculation. In children about 5 years old, the age when reinforcing doses are usually given, cases provoked by inoculation probably formed only 2% of the total. The period of highest risk was the second quarter of the year. A clear relation between the site of inoculation and the site of paralysis was demonstrated. No evidence was found to support the belief that children said to have been inoculated subcutaneously were less liable to develop paralysis than children said to have been inoculated intramuscularly. There was no evidence that virus was being transmitted from child to child via syringes. In 1954 and 1955 a modified investigation was made, and the relation between site of inoculation and site of paralysis was again demonstrated. The mechanism by which inoculation acts is a matter for conjecture, but the evidence submitted leaves no doubt that it predisposes to the occurrence of paralysis and does not act merely by determining the site of paralysis. These findings raise practical problems that have to be considered in the inoculation of children with whooping-cough vaccines and diphtheria toxoids, singly or in combination.

Studies on Headache: Central Versus Peripheral Action of Ergotamine Tartrate and Its Relevance to the Therapy of Migraine Headache. E. Pichler, A. M. Ostfeld, H. Goodell and H. G. Wolff. A. M. A. Arch. Neurol. & Psychiat. 76:571-577 (Dec.) 1956 [Chicago].

Investigations were carried out to ascertain whether the amount of ergotamine tartrate usually administered for migraine headache, approximately 0.007 mg. per kilogram of body weight, has a significant central effect in blocking or diminishing vasomotor reflexes. Eleven healthy young men and 2 patients with cervical sympathectomy and stellate ganglionectomy served as subjects. The carotid sinus reflex, the "cold pressor" response, and levarterenol-induced hypertension and bradycardia were used as indicators of possible central nervous system effects of ergotamine tartrate in 3 series of experiments. In a 4th series the effect of ergotamine tartrate on ostensibly sympathectomized cranial arteries was studied.

The experiments revealed evidence of a prompt and striking peripheral vasoconstrictor action and a lack of central action of ergotamine tartrate in causing vasoconstriction. After the intravenous administration of ergotamine tartrate, marked peripheral vasoconstriction preceded sensations of nausea by 15 or more minutes. The administration of ergotamine tartrate did not prevent the elevation of the blood pressure during the cold pressor reaction. The sensitivity of the carotid sinus reflex was not altered even during the period of nausea following administration of ergotamine tartrate. The bradycardia accompanying the infusion of levarterenol occurred as predictably after the administration of ergotamine tartrate as before. The administration of Hydergine (3 dihydrogenated ergot alkaloids) either before or after the administration of ergotamine tartrate did not alter the vasoconstrictor effect of the latter agent. In 2 subjects with ostensibly sympathectomized extracranial arteries, the peripheral vasoconstrictor action of ergotamine tartrate was as effective as in intact subjects. It is concluded that in terminating a migraine headache attack the action of ergotamine tartrate is peripheral and that in the amounts therapeutically administered to human subjects central effects are not significant.

Pearly Tumours in Relation to the Central Nervous System. J. S. Tytus and J. Pennybacker. J. Neurol. Neurosurg. & Psychiat. 19:241-259 (Nov.) 1956 [London].

Observations are presented on 41 patients with pearly tumors related to the nervous system. This term includes epidermoids and dermoids, since, in spite of their difference histologically, their characteristics are quite similar. Two patients had pericranial dermoids unassociated with neurological abnormalities. Six patients had orbital pearly tumors, with proptosis as the main complaint. Visual disturbances were minimal. The main indication for surgical removal of these growths is cosmetic. Six patients had pearly tumors

arising in the petrous bone and presented with peripheral facial weakness, associated with deafness in 5 cases. Operations were carried out in 4, but improved facial nerve function occurred in only 1. Earlier operation should improve these results. The features of the diploic pearly tumors are discussed and 2 examples cited.

Two patients had pearly tumors arising in the suprasellar region and presented with a chiasmal syndrome unassociated with endocrine abnormalities. Radiographs of the sella turcica were normal. Total removal of these tumors is hazardous because of their relation to the optic nerves and internal carotid arteries. Intracapsular removal is probably preferable, since they recur slowly. Seven patients had intracerebral pearly tumors. Epilepsy featured in the history of 4. Three patients had cerebellopontine angle epidermoids and presented with the usual features of tumors in this region. Eight patients had pearly tumors arising in the vermis and 4th ventricle. Three of them had associated dermal sinuses. Their role in the production of meningitis is emphasized, along with the importance of early surgical intervention.

Seven patients had intraspinal (intradural) pearly tumors, 6 of which were at least in part intramedullary. Associated dermal sinuses were present in 2 patients, 1 of whom presented with meningitis. When these growths are entangled in the cauda equina or when they invade the spinal cord, incomplete removal seems advisable to prevent further damage to these structures. All of the patients with extradural pearly tumors survived operation, and there have been no recurrences in this group. Of the 27 patients with intradural tumors, 4 died in the immediate postoperative period. Three of these deaths occurred in patients in the cerebellar group and were attributed, at least in part, to late surgical intervention. The other occurred in a patient with a cerebellopontine angle epidermoid. Aseptic meningitis occurred in 10 patients with intradural pearly tumors. Repeated spinal fluid cultures were sterile in 8 cases. Two patients developed a bacterial meningitis, which was fatal in 1. Although removal was incomplete in at least 12 patients with intradural pearly tumors, recurrence has taken place in only 2, 4 and 13 years postoperatively.

Autohemotherapy—An Effective Treatment for Herpes Zoster. F. J. Ansfield and J. L. Rens. Wisconsin M. J. **55**:1319-1320 (Dec.) 1956 [Madison].

The authors treated 54 cases of herpes zoster by intramuscular injections of 15 cc. of the patient's own blood. The diagnosis was established in each case after the typical herpes vesicles made their appearance and the distribution of the lesions involved the usual locations—occipital, thoracic, abdominal, lumbar, or extremity. Then 15 cc. of blood was drawn from the antecubital vein of the patient and injected deep into the gluteal muscle on one side. The patient was instructed to return in 48 hours. If the pain had subsided, no further treatment was given. This was the case in 8 patients. If the pain was still present after 48 hours, the patient was given a similar injection into the opposite gluteal muscle. Thirty-four patients were cured 48 hours after this 2nd injection. Twelve patients who still had painful herpes zoster were given a 3rd injection of 15 cc. of their blood and instructed to return in 48 hours. In 10 of these 12 patients the pain had subsided and the vesicles were clearing rapidly 2 days after the 3rd injection, but 2 patients failed to respond to all 3 injections. One of these patients was given 2 injections of 1,000 mcg. of vitamin B_{12}, which apparently arrested the pain promptly. The other patient was likewise given vitamin B_{12} injections following failure to respond to autohemotherapy, but there was no response to vitamin B_{12} either. The pain gradually subsided spontaneously during the next 3 months. The authors feel that these results are unsurpassed and urge that autohemotherapy be used routinely in treating herpes zoster.

GYNECOLOGY & OBSTETRICS

The Results of Treatment of Ovarian Cancer with One Million Volt X-ray. F. C. H. Chu. Surg. Gynec. & Obst. **104**:45-52 (Jan.) 1957 [Chicago].

This report reviews observations on 112 patients with proved ovarian cancer treated by 1,000 kv. of irradiation between January, 1949, and August, 1953. Sixty of these patients were referred for irradiation in the immediate postoperative period. The remaining 52 patients were treated for recurrences, 13 having been treated by surgery only (one or several interventions), 34 having received surgery and irradiation, and 5 having been treated with triethylene melamine (TEM) plus irradiation or other drugs plus irradiation. Irradiation has definite value in the management of ovarian carcinoma. Radiation has been considered an important adjunct to surgery, and even in advanced cases, in which definitive surgery is not feasible, radiation has given palliation, subjective or objective, with an average duration of about 9 months in approximately two-thirds of the cases. The results of radiation obtained in this study would appear to indicate that a tumor dose of 3,000 to 5,000 r in 3 to 6 weeks gives a better chance of response than a lower dosage. It is possible to deliver a higher midplane dose to large ports with supervoltage therapy than it is with conventional x-ray energies. The solid and the mixed solid and papillary types of serous adenocarcinoma are more malignant than the papillary type, but no significant difference in the responsiveness to irradiation was noted.

Most of the patients in whom the irradiation was applied through pelvic ports or small abdominal ports tolerated the treatment fairly well. Almost all patients who had irradiation of the whole abdomen developed radiation reactions of varying degrees, including some mild nausea, vomiting, diarrhea, and weakness. Symptoms of such severity that the radiation had to be discontinued developed in 6 patients. One patient experienced an exacerbation of ulcerative colitis and died. Transitory leukopenia developed in 2 patients. Skin reaction was never a real problem, most patients having only an erythema and dry peeling. A moist desquamation in the inguinal and gluteal folds de-

veloped in a few patients. In view of the fact that severe systemic reactions do occasionally occur, the question arises whether irradiation for palliation is worthwhile. It is necessary to individualize the approach in each patient, weighing carefully the value of palliation against the temporary suffering from the radiation reaction. If the plan of treatment is flexible and the complications are managed properly and promptly, most patients tolerate the desired dose. When the reactions are severe it is necessary to halt the radiation therapy, and other forms of therapy have to be considered.

Renal Biopsies from Patients with "Toxemia of Pregnancy." W. J. Dieckmann, E. L. Potter and P. MacCartney. Am. J. Obst. & Gynec. 73:1-16 (Jan.) 1957 [St. Louis].

Satisfactory renal biopsies were obtained on 71 pregnant patients with toxemia. Twenty-six patients were primigravidas, 44 multigravidas, and 1 was a nonpregnant multipara. The diagnoses based on renal biopsies were made without knowledge of the clinical condition. Moderate or severe changes in renal glomeruli were present in all primigravidas with symptoms of preeclampsia, in 2 of 3 with eclampsia, in 5 of 7 with hypertensive disease, and also in 6 of 26 multigravidas with hypertensive disease. The changes consisted of thickening of basement membrane, the presence of fibrils in endothelial cells, and the narrowing of glomerular capillaries. This lesion is most constant in primiparas with preeclampsia, but it may occur in patients with any variety of toxemia of pregnancy. A mild change—slight thickening of basement membrane, slight fibrillation in endothelial cells, and little reduction in capillary lumens—occurred in 1 primigravida with eclampsia, in 3 patients with glomerulonephritis, in 13 multigravidas with hypertensive disease, and in 4 with normal pregnancies. This mild lesion occurs rarely in preeclampsia and is more frequent in multigravidas with hypertensive disease.

The Role of the Fibrinolytic Enzyme System in Obstetrical Afibrinogenemia. L. L. Phillips, G. Montgomery Jr. and H. C. Taylor Jr. Am. J. Obst. & Gynec. 73:43-56 (Jan.) 1957 [St. Louis].

The authors report on 10 patients with obstetric afibrinogenemia. The patients with levels below 55 mg. per 100 cc. received fibrinogen intravenously in quantities of 2 or 3 gm. in order to control postpartum hemorrhage. Two patients with levels at approximately 75 mg. per 100 cc. did not require fibrinogen therapy. Two patients with higher levels (89 and 170 mg.) were given fibrinogen, because the alarming hemorrhage did not respond to treatment with whole blood and oxytocics. After fibrinogen therapy was instituted, bleeding showed a remarkable decrease within 30 to 60 minutes and changed to normal lochia within 3 hours. Fibrinogen levels rose to 120 mg. per 100 cc. The enzyme activities returned to normal levels and the inhibitor levels increased. The serially collected blood samples were studied for fibrinogen levels and for the various factors of the fibrinolytic enzyme system. Small but significant levels of fibrinolytic and/or fibrinogenolytic activity were found. The presence of an active proteolytic enzyme in the blood may be partially responsible for the low levels of fibrinogen in patients with obstetric afibrinogenemia.

Problems Associated with Toxemia in Twin Pregnancies. M. J. Bulfin and P. E. Lawler. Am. J. Obst. & Gynec. 73:37-42 (Jan.) 1957 [St. Louis].

Two hundred thirty-four sets of twins have been delivered, beyond 7 months' gestation, from 1950 to 1955 at the Little Company of Mary Hospital, Chicago. Seventy-three mothers (31.2%) had toxemia. The authors made separate studies of the primigravid and multigravid patients. Thirty-six of 50 primigravidas (72%) and 37 of 184 multigravidas (20.1%) with twin pregnancies were toxemic. The fetal death rate in primigravidas was 8.45% and in multigravidas 1.3%. Pitocin was given for induction of labor, but it was less efficacious in twin than in single pregnancies. Seven patients had severe postpartum hypertension, which was controlled with Serpasil. Ergotrate should be withheld in toxemic pregnant patients because of its hypertensive effect. Primigravid patients with hypertensive disease should be watched very closely and examined by x-ray at 6 months' gestation. Precautionary measures against development of toxemia should be taken if twins are present.

Pregnancy Complicated by Diabetes Mellitus: A Review of 119 Cases. A. E. M. Stevenson. Brit. M. J. 2:1514-1518 (Dec. 29) 1956 [London].

Eighty-nine women with diabetes mellitus had 119 pregnancies for which they were treated at the Royal Maternity Hospital in Belfast, Ireland, in the course of the past 16 years. Sixty-seven of the 119 pregnancies occurred between 1940 and 1950 and 52 between 1951 and 1955. Eighty-eight of the 89 women survived and 1 died. Thirty-seven fetuses died, a total fetal loss of 30.8%. The deaths of 24 (35.4%) of these fetuses occurred between 1940 and 1950 and the deaths of 13 (25%) between 1951 and 1955. The total fetal loss, excluding abortions, for the past 5 years, was 19%. Six of the 37 fetal deaths occurred before 28 weeks of pregnancy; 4 of the 6 were spontaneous abortions; hysterectomy was performed on 1 mother at 26 weeks because of severe diabetes and impaired renal function; and the 6th fetal death occurred in the only mother who died undelivered. Twenty-two fetal deaths occurred after 28 weeks of pregnancy, and the remaining 9 deaths were neonatal.

The following facts must be born in mind in planning the management of pregnant women with diabetes mellitus: the fetus is liable to die in utero, and the risk of intrauterine death increases as term approaches. Toxemia, diabetic coma, and a persistently poorly controlled diabetic state have a harmful effect on the fetus. A clinical trial into the use of hormones in pregnant women with diabetes mellitus was conducted by the British Medical Research Council in

1955. It showed that hormone therapy in its present form does not reduce fetal mortality. There is no known method that will prevent intrauterine death and allow pregnancy to go to term. Management of the pregnant diabetic patient should include (1) teamwork by obstetrician, physician, and pediatrician of the highest order; (2) accurate control of maternal diabetes mellitus, and this implies strict antenatal care from the beginning of pregnancy; (3) admission to hospital at the 28th week, or earlier if stabilization is unsatisfactory; (4) premature delivery at 35 weeks, or earlier if indicated; (5) delivery by cesarean section in all primigravidas and all but a few multigravidas; and (6) skilled nursing in a modern nursery unit.

Blood Coagulation During Normal Pregnancy, Labor, and the Puerperium. A. L. Kennan and W. N. Bell. Am. J. Obst. & Gynec. **73**:57-64 (Jan.) 1957 [St. Louis].

Twenty normal pregnant patients, 12 multiparas and 8 primiparas, were followed from their 34th week of gestation through delivery and the early part of puerperium. A complete coagulogram of each patient was carried out in duplicate during late pregnancy, labor, and puerperium. A decrease in fibrin and platelets occurred within the last 7 days before delivery. The increase of platelets during labor in most of the patients was reflected in a proportionate increase of prothrombin consumption and faster clot retraction. Fibrinogen appeared to be utilized for hemostasis. The changes that occurred during the puerperium seemed to result from a reparative stimulus consisting of the increased ability of the blood to clot. There is an apparent sudden decrease in the plasma volume, which approaches the predelivery value. With the beginning postpartum diuresis the plasma volume gradually returns to the prepregnancy level. The hematocrit determinations carried out by the authors support the thesis that the changes during puerperium contributed to the increase of the clotting factors. There was a definite increase in the coagulation factors associated with the loss of plasma volume.

A Case of Prolonged Pregnancy and a Review of the Literature on Superfoetation in an Endeavour to Explain the Phenomenon. I. R. Milne. Central African J. Med. **2**:385-389 (Nov.) 1956 [Salisbury].

Milne presents the history of a woman who had a pregnancy lasting 383 days, or 103 days beyond the estimated date of delivery, based on the last menstrual period. The history suggested a second ovulation occurring 79 days after the last menstrual period with interruption of the pregnancy at that time, with a second nidation occurring within a week of this date. The phenomenon caused the author to consider superfetation to account for the prolongation of pregnancy. In view of the weight of the infant at birth, 5 lb. 12 oz. (2,600 gm.), a second ovulation and a second pregnancy seemed the most likely explanation. It was possible to disprove a bicornuate uterus during a classical cesarean section.

PEDIATRICS

Early Diagnosis of Juvenile Amaurotic Idiocy: Lipoid Lymphocyte Degeneration. K. Gilje and A. J. Nissen. Tidsskr. norske lægefor. **76**:855-856 (Nov. 15) 1956 (In Norwegian) [Oslo].

Juvenile amaurotic idiocy, in addition to degeneration in the nerve cells, causes degeneration in the lymphatic system, spleen, lymph nodes, and in the lymphocytes of the blood. The prognosis is unfavorable. The disease hereditary, with recessive inheritance. The impairment of vision is moderate in early childhood but increases toward amaurosis when the child approaches puberty. At the age of 10 to 12 years, increasing mental changes are seen and epileptic attacks occur. Marked changes in pigment and atrophy of the optic nerve appear at a later stage. The diagnosis depends on failing vision, epileptic seizures, and increasing dementia, which are late symptoms and the result of progressive lipoid degenerative changes in retina and cerebrum. Retinal degeneration was established in 14 of the 60 pupils in the Dalen Public School for the Blind in Trondheim. Examination of the blood in the 14 patients revealed lipoid degeneration of lymphocytes in 6. Closer study of these patients showed progressive failure of vision and increasing dementia, with epilepsy in 4. The cases occurred sporadically. Nine of 10 cases of the disease previously described by Nissen occurred in 3 groups of siblings. Investigation of lipoid degeneration of lymphocytes is believed to be an adjuvant in the possible diagnosis of juvenile amaurotic idiocy at an early stage.

Genetic, Clinical, Biochemical, and Pathological Features of Hypophosphatasia: Based on the Study of a Family. R. A. McCance, D. V. I. Fairweather, A. M. Barrett and A. B. Morrison. Quart. J. Med. **25**:523-537 (Oct.) 1956 [Oxford, England].

In 1948, Rathbun described what appears to have been a new developmental anomaly under the title of hypophosphatasia. A boy who was 3 weeks old on admission was found to have multiple abnormalities and defective mineralization of the skeleton, with a serum calcium level of 13.6 mg. per 100 ml. and a plasma phosphatase level that varied from 0 to 0.7 units, compared with the normal range of 5 to 15 units. The picture that emerged from the report by Rathbun and from several other papers on this anomaly appears to be that of a familial disease characterized by hypophosphatasia. Studies are reported on a girl and boy (siblings) who died of hypophosphatasia in early life. The skull, ribs, and long bones were very abnormal radiologically. Clinically the limbs were deformed, and the wrists, ribs, and fontanelles were somewhat like those in severe rickets. The biochemical findings included a high level of calcium and a low level of alkaline phosphatase in the serum and the excretion of phosphoethanolamine and probably adenosine monophosphate in the urine. After death, a subnormal activity of alkaline phosphatase was demonstrated in the liver, kidney, and intestine, and especially in the bones, which were also largely uncalcified. Histologi-

cally, the bones contained much uncalcified osteoid tissue, and the kidneys had abnormal tubules and deposits of calcium.

The family tree of these children was traced as far back as possible, and studies were made on some of the members of the family. The father and paternal grandfather were found to have low levels of serum alkaline phosphatase but to be clinically normal. The primary morphological abnormalities in the bones of the babies—deficiency of calcification, excess of osteoid tissue, and irregularity of endochondral ossification—appear to be identical with those seen in rickets. Morphological features not seen in rickets were extreme softness of the skull and shortness of the ribs and the long bones, and the peculiar shape of the costochondral junctions. The earlier onset and greater severity of the defect in hypophosphatasia may explain the difference. Deficient calcification is the predominant feature of the bones in hypophosphatasia, just as it is in rickets. The cause of the defective calcification is different, however, from that in rickets, and the authors believe that the 2 disorders should be clearly distinguished. Rickets is characterized biochemically by a high level of alkaline phosphatase activity in the serum and usually by low levels of inorganic phosphorus and calcium, all of which are restored to normal by giving vitamin D. For the disease described here the authors accept Rathbun's term, hypophosphatasia. While the patients with mild cases of hypophosphatasia seem to recover, there is no specific cure. It is probably beneficial to the kidneys to keep the hypercalcemia under control if it is possible to do this by dietary or other means, but it seems illogical to advocate the administration of vitamin D. The skull, and later the long bones, may require operative treatment.

Primary Vitamin-D Resistant Rickets: III. Biophysical Studies of Skeletal Tissue. B. Engfeldt, R. Zetterstrom and J. Winberg. J. Bone & Joint Surg. **38-A:**1323-1334 (Dec.) 1956 [Boston].

There is evidence that primary vitamin-D-resistant rickets is genetically determined, but its pathogenesis remains obscure. Bone biopsy specimens were obtained from 4 patients with this disorder: 2 boys aged 6 and 3 years and 2 3-year-old girls. The mineral distribution in different bones, the organization of the collagen bundles, and the ultrastructure were studied by various biophysical methods as well as by ordinary histological means. It was found that structural features in this disease differ from those found in ordinary rickets. Compact bone showed structural changes resembling those found in osteitis deformans. These changes are characterized by an abnormal mosaic-like pattern of bone that is not affected by large doses of vitamin D. Histological examination of the costochondral junction of these patients, however, revealed abnormalities similar to those found in ordinary vitamin-D-deficiency rickets.

The process is apparently more complicated than in vitamin-deficiency rickets. The balance between new deposition of bone minerals and resorption processes seems to be impaired. The extremely low serum phosphorus level probably indicates that the pathological process is not solely connected with skeletal metabolism but also involves the organs regulating calcium and phosphate metabolism. Albright and his associates have given evidence of secondary hyperparathyroidism being present in vitamin-D-resistant rickets. There is a possibility that the existing secondary hyperparathyroidism not only modifies the blood chemistry but also exerts an influence on the skeletal disorder. Thus at least some features of the morphological changes of the skeletal tissue in vitamin-D-resistant rickets could possibly be attributed to disturbed parathyroid function. It may be concluded that vitamin-D-resistant rickets is a well-defined, genetically determined clinical and pathological entity, different from ordinary rickets. Treatment with vitamin D in massive doses has no direct effect on the skeleton in vitamin-D-resistant rickets. It improves the possibilities for a deposition of mineral salts in the skeleton by its hypercalcemic effect but does not influence the morphology of the skeletal disorder and does not cure the disease.

Constitutional Methemoglobinemic Cyanosis: Description of One Case. P. C. Gamalero and G. Bono. Minerva pediat. **8:**1307-1312 (Oct. 27) 1956 (In Italian) [Turin, Italy].

Constitutional methemoglobinemia is characterized by the presence of an abnormal amount of methemoglobin in the circulation that is not related to endogenic or exogenic causes. The symptoms can be present at birth, they can appear during the first months of life, or, very rarely, they appear later in life. The case is described of a 2-year-old boy with cyanosis and bluish discoloration of the mucous membranes since the first weeks of his life. The symptoms were more evident every time the child cried. Clinical and laboratory tests did not show the presence of congenital cardiopathy. Investigation of the child's history as well as chemical analysis of the water used by him did not reveal the presence of toxic elements. The child was treated for a week with 2 daily injections of 200 mg. each of vitamin C. Subsequently, 500 mg. of vitamin C was given daily by mouth. This treatment given in cycles, alternated with periods of rest, produced a marked reduction in the intensity of the cyanosis. The symptoms tended to increase every time the treatment was suspended.

DERMATOLOGY

Eosinophilic Granuloma of Skin and Mucous Membrane: Association with Diabetes Insipidus. R. B. Kierland, J. G. Epstein and W. E. Weber. A. M. A. Arch. Dermat. **75:**45-54 (Jan.) 1957 [Chicago].

Three women between the ages of 29 and 50 years, one 2-year-old girl, and one 42-year-old man are reported on in whom characteristic, deep, sharply delineated, ulcerated, granulomatous lesions involving the skin of the inguinal, perianal, perineal, and vulval regions and buccal mucous membrane were observed. The diagnosis of eosinophilic granuloma was made with the aid of microscopic examination of tissue from the mentioned sites. Diabetes insipidus was noted in the 4 adult patients and dermatitis of an inflammatory and seborrheic nature in 2 women and in the child. Two women had skeletal lesions resembling those of

eosinophilic granuloma and lipid histiocytosis of cholesterol type (Hand-Schüller-Christian disease) and Letterer-Siwe's disease. The laboratory studies were not of diagnostic significance except for the low specific gravity of the urine. Treatment included supportive, anti-inflammatory, and antibacterial measures. Roentgen therapy was employed as a more or less specific treatment. Two patients obtained considerable improvement, 1 had a mild recurrence, and 2 got some transitory relief, but the treatment at best was only palliative. One patient received a short course of cortisone with no benefit. One patient was given nitrogen mustard with no relief. One patient was given 1 mg. of triethylene melamine daily for about 18 months; she had no cutaneous or oral lesions for 6 months. Vasopressin tannate was effective in controlling the diabetes insipidus of all 4 patients.

These patients seemed to have characteristic disturbances that belong to the disease group including eosinophilic granuloma, lipid histiocytosis of cholesterol type, and Letterer-Siwe's disease, and they add to the evidence for a common basic process for these entities.

Leprosy and Tuberculosis: Antagonistic Diseases. J. M. M. Fernandez. A. M. A. Arch. Dermat. **75**:101-106 (Jan.) 1957 [Chicago].

Fernandez discusses his hypothesis that leprosy and tuberculosis are antagonistic diseases from the immunologic, clinical, and epidemiological points of view. His immunologic arguments are based on the fact that a spontaneous tuberculous infection, or one induced by BCG inoculation, exercises a positivizing influence on the reaction of the skin to lepromin. Granted that a positive reaction to lepromin in patients with leprosy means good resistance to the disease, this also means that the tuberculous factor obstructs or inhibits the pathological action of Mycobacterium leprae. The author's clinical arguments are based on the comparative study of the development of leprosy in 3 groups living with persons with leprosy: tuberculin-negative, tuberculin-positive, and BCG-vaccinated persons. The index of infection and the malignancy of the disease in those becoming infected was much greater in the tuberculin-negative group than in the 2 other groups. Comparative epidemiological studies of leprosy and tuberculosis carried out by other workers in different countries showed that the leprosy index is lower in a country the population of which has high tuberculous index and vice versa.

An investigation made by the author in 1946 among 190 marriage partners of patients with leprosy in Rosario, Argentina, revealed 38 contact cases (20%). Thirty-three (87.1%) of the 38 persons were tuberculoid and 5 (12.8%) lepromatous. These data coincide with those obtained by other authors in different countries and are in favor of the antagonistic action between leprosy and tuberculosis; the tuberculin-positive persons predominate among the marriage partners exposed to infection, and their previous infection with tuberculosis protects them. The importance of the author's theory of an antagonistic action between leprosy and tuberculosis is emphasized, and a plan of work to confirm or disprove it is suggested.

UROLOGY

Hypertrophy of Prostate: Experiences with 250 Transvesical Prostatectomies. R. Andersen. Tidsskr. norske lægefor. **76**:863-867 (Nov. 15) 1956 (In Norwegian) [Oslo].

Andersen finds that transvesical prostatectomy maintains its place among other operations for prostatic disorders. In 250 consecutive transvesical prostatectomies from 1946 to 1955, the operative mortality was 1.6% in spite of the age of the patients (average age, 67) and the consequently more frequent complicating diseases. Even more serious cardiac affections and diabetes are not contraindications if they are well controlled. Gauze packing of the prostatic bed with suprapubic drainage through a Malecot catheter was applied in the first 24 cases, Foley bag catheter for hemostasis with suprapubic drainage through a Malecot catheter in 114 cases, and Foley bag catheter per urethram with primary closure of the bladder in 112 cases (Harris' operation). The mortality for the patients operated on by the Harris method was less than 1%. This method seems to give fewer postoperative complications, more rapid mobilization, shorter period of hospitalization, and fewer late complications. Postoperative obstruction occurred in 11 patients, or 4.4%; in 10 of these transurethral and in 1 transvesical reoperation was done, with good permanent result. Ventral hernia in the operative wound developed in 2 instances.

Unilateral Nephrectomy in Hypertensive Disease. H. W. Smith. J. Urol. **76**:685-701 (Dec.) 1956 [Baltimore].

A review of the literature shows that from 1937 to 1956 a total of 575 unilateral nephrectomies have been performed in hypertensive patients with demonstrated or suspected unilateral impairment of renal function. The blood pressure has been reduced to 140/90 mm. Hg or below for 1 year or longer in 26%. This indicates that unilateral renal disease, amenable to surgical correction, can cause either benign or accelerated hypertensive disease in man. The record is unsatisfactory in 2 respects: the follow-up period on many patients was less than 1 year, and probably many negative results were not reported. The true incidence of hypertensive vascular disease (elevated diastolic pressure) in man is unknown, but records on living subjects indicate that this figure is about 25% of persons from the 3rd to the 7th decade of life. In the rest of the population the diastolic pressure remains below 90 mm. Hg throughout life and may tend to decrease with age. The cause of hypertensive vascular disease remains unknown. The kidneys cannot be indicted: arteriolar disease appears to be primary, and the renal circulation and parenchyma become involved secondarily, as is the case in other organs.

Our knowledge of hypertension is in a state of flux. Probably less than 2% of patients with hypertensive vascular disease are candidates for therapeutic renal surgery. Patients who have been subjected to renal surgery for correction of hypertensive disease should be followed for a minimum of 1 year and the diastolic pressure reduced to or below 90 mm. Hg before they are classified as cured. Nevertheless, renal surgery

(generally nephrectomy), even though limited in applicability, is the only demonstrated apparently permanent cure for so-called essential hypertension. Urologic examination is indicated in hypertensive patients only when strong suspicion is raised by history, physical examination, and routine laboratory examination. The decision to perform nephrectomy must rest on definite indications, not on the mere hope of reducing blood pressure. In general, this conservative attitude has prevailed, but the pendulum appears to be swinging toward what may prove to be undue optimism and the sacrifice of useful and perhaps vitally needed kidneys that are not responsible for the hypertension. The urologist may find himself pressed to intervene surgically against his better judgment. Even in the presence of obvious unilateral disease, nephrectomy remains an experimental procedure and subject to failure.

Newer Concepts of the Klinefelter Syndrome. R. G. Bunge and J. T. Bradbury. J. Urol. **76**:758-765 (Dec.) 1956 [Baltimore].

The Klinefelter syndrome is characterized by bilateral gynecomastia, small testes, aspermatogenesis, evidence of normal to moderately reduced function of the Leydig cells, increased excretion of follicle-stimulating hormone, and usually a reduced excretion of 17-ketosteroids. The authors describe studies on 8 patients with this syndrome. A positive (female) chromatin test was obtained from oral smears in each of the patients. Special studies were made of 3 patients. A gonad was removed from each, and histological examination yielded evidence of spermatogenesis, which had not been revealed in biopsy specimens. It is suggested that the cause of this syndrome is a bilateral embryonic ovarian cortical failure and that hermaphroditismus verus lateralis may represent a unilateral embryonic ovarian cortical failure. The hormone production by the testes of patients with Klinefelter's syndrome needs further evaluation.

OTOLARYNGOLOGY

Quinsy. N. Young. Practitioner **177**:674-678 (Dec.) 1956 [London].

A quinsy, a peritonsillar abscess, is always a complication of tonsillitis. Although it is the natural habit of the tonsil to nurture species of organisms, at times such virulent ones are deposited on its surface that the superficial defences are overwhelmed, the invaders occupy the crypts, and areas of epithelium are destroyed. This causes clogging of the outlets by debris, pus, and granulations, so that small abscesses form in the interstices of the tonsil. Each act of swallowing or coughing contracts the mouths of the crypts, but if there is sufficient obstruction this cannot occur, and in the course of time one of two things happens—either the abscess becomes encapsulated and the crypts closed off by scar tissue, or the abscess extends more deeply along the branches. In the first instance, a state of chronic tonsillitis is established; in the second a quinsy may accrue—by pus eroding the capsule and coming to lie between it and the muscular coat. In the differential diagnosis of quinsy such conditions as neoplasm, Vincent's angina, diphtheria, foreign body, gumma, tubercle, agranulocytosis, mononucleosis, leukemia, tetanus, and alveolar abscess must be excluded.

Medical treatment is similar to that for primary tonsillitis and should be continued until the necessity for surgery becomes obvious. Rest—of the patient, by confinement to bed in a well-ventilated room of even temperature, with freedom from worries and tiresome visitors; and of the parts, by "splinting" the neck, in a comfortable decongestive position—is an essential part of treatment. The patient should be nursed sitting up, so that swallowing, breathing and coughing are easier. Hot alkaline mouthwashes will help to dissolve the thick glairy saliva, so painful to dispel. Toxemia should be combated by eliminatory measures, constipation being common, and by dilution through large quantities of bland drinks. Sulfonamides or antibiotics will have been utilized since early in the illness. If progress is less than satisfactory after 10 days' adequate therapy, the diagnosis must be revised and surgery considered. The author comments on the difficulties of anesthesia in quinsy and describes his surgical technique. A tonsil damaged by a peritonsillar abscess and its surgical evacuation is vulnerable to further quinsies, and its removal is the only safeguard against these. Prophylactic tonsillectomy should be carried out only after a certain interval.

THERAPEUTICS

Two New Antibiotics: Antibacterial Activity of Novobiocin and Vancomycin. R. W. Fairbrother and B. L. Williams. Lancet **2**:1177-1178 (Dec. 8) 1956 [London].

Fairbrother and Williams investigated the in vitro activity of 2 new antibiotics: Vancomycin (Vancocin), prepared from cultures of Streptomyces orientalis, and novobiocin (Albamycin, Cathomycin, or Cardelmycin), prepared from different species of streptomyces. Tests to determine the sensitivity of the common pathogens to the new antibiotics were carried out by 2 standard methods: (1) the dried-disk technique and (2) serial dilution. All the organisms were freshly isolated from infective processes. In the disk technique, 50 mg. of Vancomycin and 10 mg. of novobiocin per disk were used to test a total of 1,350 organisms against Vancomycin and 1,100 organisms against novobiocin. The serial-dilution technique ascertained the minimum inhibitory concentration (micrograms per milliliter) of novobiocin against 177 organisms and of Vancomycin against 105 different organisms. The results of the sensitivity tests indicate that Vancomycin and novobiocin are active against most gram-positive cocci and should be particularly valuable in the treatment of infections caused by penicillin-resistant micrococci (staphylococci). Little or no activity against the gram-negative bacilli, usually associated with urinary infections, was found.

The authors admit that in vitro sensitivity tests do not provide an absolute criterion of clinical efficiency; they only indicate the activity of the antibiotic under laboratory conditions, which tend to be favorable to the antibiotic. Carefully controlled clinical trials are necessary before a final assessment of novobiocin can

be given, particularly in the treatment of Proteus infections. Novobiocin-resistant strains of Micrococcus aureus have already been isolated, and this antibiotic should not be used indiscriminately. The extending range of antibiotics is making the selection of the most suitable agent for a particular infection a difficult matter. Laboratory control of these substances is becoming increasingly important.

A Comparison Between Protoveratrine A and Protoveratrine B Orally in Arterial Hypertension: A Therapeutically Important Difference in Activity. B. M. Winer. New England J. Med. **255**:1173-1179 (Dec. 20) 1956 [Boston].

The hypotensive activity of protoveratrine A and, separately, that of protoveratrine B were studied in 13 patients given the drugs orally. Three preparations of each alkaloid were used. Two consisted of the alkaloids in tablet form, prepared in different concentrations and assayed by different pharmaceutical houses by physicochemical means. The 3rd consisted of the individual alkaloids in a liquid form prepared for parenteral use. The "parenteral" preparations had been previously studied and found to have nearly equal hypotensive potency intravenously. A mixture of protoveratrines A and B, containing 53% protoveratrine A $\pm 2\%$, was also given orally to 6 of these patients. An unequivocal quantitative difference in hypotensive activity has been established between protoveratrine A and protoveratrine B when the substances are given orally. Protoveratrine A is a potent hypotensive agent with a narrow therapeutic dosage range. It is the major active principle in mixtures of protoveratrines A and B given by mouth. The use of protoveratrine A instead of a mixture of protoveratrines A and B would remove one factor affecting the variability of response to oral protoveratrine therapy. Nonetheless, the satisfactory use of any veratrum preparation requires critical attention to dosage and consideration of cumulative effects.

Protoveratrine B is inactive orally in doses several times the hypotensive doses of protoveratrine A. Preliminary studies of divided doses of more than 10 mg. a day indicate that protoveratrine B has strong hypotensive activity, which may be prolonged and not accompanied by emetic effects. Unusual side-effects related to muscle function have appeared, resembling clinical myotonic syndromes. These studies have provided definite evidence of the value of the use of single pure alkaloids rather than a mixture. Further studies of pure veratrum alkaloids are indicated.

Intra-arterial Oxygen in Peripheral Vascular Disease. R. J. Marshall and R. F. Whelan. Brit. M. J. **2**:1448-1451 (Dec. 22) 1956 [London].

Marshall and Whelan describe circulatory changes induced by intra-arterial oxygen injections in 18 patients with peripheral arterial disease involving upper and lower limbs. The changes are compared with those following intra-arterial injection of 3 potent vasodilator drugs: tolazoline (Priscol), hydralazine (Apresoline), and phenylisobutyl-n-p-hydroxy ephedrine (Dilatal). In most patients the injections resulted in an increase in blood flow lasting for 24 to 60 hours. In the same patients injections of tolazoline, hydralazine, and Dilatal caused only relatively transient increases in blood flow. The administration of oxygen has been a relatively safe procedure.

The injections are made with the patient horizontal, and the injected limb is held slightly raised to guard against the possibility of gas emboli spreading proximally against the current of arterial blood and causing visceral infarction. The possibility exists that, in patients with degenerative arterial disease, injections may cause local damage to the arterial wall or dislodge material from atheromatous plaques. Care is taken to make each injection at a different site and to use a sharp short-bevel needle, 1 mm. in external diameter. If proper precautions are taken, the intra-arterial injection of oxygen is a safe procedure. It should not, however, be used in patients with very low resting blood flows or in those with recent occlusion of a major vessel. Occasionally the paradoxical effect of reduction in blood flow through the foot may be observed to follow intrafemoral injection of oxygen, but this effect is also apt to occur with any other potent vasodilator substance. It is concluded that oxygen should be used in preference to other vasodilators in the treatment of peripheral vascular disease by intra-arterial injections.

A New Antibiotic: The Use of RO 2-7638 in Diphtheritic Infection. B. Gagliardi. Minerva med. **47**:1431-1435 (Oct. 31) 1956 (In Italian) [Turin, Italy].

The author studied the effects of RO 2-7638, a new antibiotic known in the United States as PA 105, on 73 patients with diphtheria (35 female and 38 male). RO 2-7638 is well tolerated and has a marked effect on gram-positive bacteria and a partial effect on gram-negative bacterial, on some rickettsias, and on some large viruses. The bacterial spectrum of this antibiotic is equal to that of penicillin, erythromycin, and carbomycin. RO 2-7638 shows little or no cross resistance with penicillin, streptomycin, oxytetracycline, chloramphenicol, chlortetracycline, polymixin B, and bacitracin; it shows cross resistance with erythromycin and carbomycin. The patients were divided into 3 groups: the first group was composed of 54 diphtheria germ carriers, the second group of 2 patients with nasal diphtheria, and the third group of 17 patients with pharyngeal diphtheria. Five patients of the first group were above 30 years of age, and the others ranged from 7 to 12 years of age. One patient of the second group was 6 years old and the other was 9 years old. Only 7 patients of the third group were of preschool age; the others ranged from 17 to 50 years of age. The nasal and pharyngeal mucus were examined when the patients entered the hospital and twice a week thereafter. The patients were dismissed only when 4 consecutive examinations had given negative results. Antibiotic treatment lasted in all patients for an average of from 5 to 6 days. Pills of 100 mg. of RO 2-7638 were used. Children of from 6 to 12 years of age received 1 pill every 3 or 4 hours, averaging a total of from 400 to 600 mg. of antibiotic per day. Adults received 6 pills per day. Children of from 2 to 6 years received 4 pills per day. The antibiotic had no untoward side-effects. The usual hos-

pitalization of from 26 to 40 days required for the patients of the first group was reduced to only 16 days in 90% of the patients. The confinement of the patients of the second group was reduced to from 22 to 28 days from the usual 40 to 48 days' confinement. Good sterilization of the oropharynx was obtained in the patients of the third group; the author does not report on the course of the disease of the patients of this group because the number of patients was small and the forms of the disease were mild.

Prolonged Glucocorticoid Therapy with Large Doses of Δ-Dehydrogenated Cortisone (Prednisone). H. H. Hennemann, D. Klaus, I. Falck and G. Volkheimer. Ztschr. ges. inn. Med. **11**:1009-1017 (Nov. 15) 1956 (In German) [Leipzig, Germany].

Prolonged treatment with large doses of prednisone was given to 4 patients, 1 48-year-old woman with acquired antibody-conditioned idiopathic hemolytic anemia, 1 68-year-old woman with lymphocytic leukemia associated with an antibody-conditioned hemolytic syndrome, 1 23-year-old woman with an adrenogenital syndrome, and 1 29-year-old woman with adrenal cortical hypofunction (Addison's disease) associated with tuberculous anterior spondylitis. The first patient with hemolytic anemia did not respond to a 5-day course of 40 mg. of repository corticotropin, but the hemoglobin level rose slowly after combined treatment with 40 mg. of repository corticotropin and 30 mg. of prednisone (Decortin) had been given daily for 5 days. Hyperglycemia and glycosuria occurred on the 10th day of this combined treatment, but this diabetes mellitus subsided when the hemolytic changes disappeared after splenectomy. An increase in the hemoglobin level and in the number of erythrocytes occurred in the 2nd patient, who had been given 40 mg. of prednisone daily for 18 days. The patient's reaction to the direct Coombs test was much less positive after 30 days of treatment with prednisone. The adrenogenital syndrome of the 3rd patient was associated with considerably increased excretion of the C-17-ketosteroids. An adrenal tumor was excluded by perirenal air insufflation. The patient first was given 50 mg. of cortisone for 3 weeks which reduced the C-17-ketosteroid excretion considerably. Ten milligrams of prednisone then was substituted for 50 mg. of cortisone, resulting in decrease of the patient's beard and increase in the hair of the head. Menstruation occurred for the first time. The patient's condition was stabilized with a daily dose of 20 mg. of prednisone, and treatment was continued ambulatorily. The patient with adrenal cortical hypofunction was given 60 mg. of prednisone daily for 2 days, 50 mg. for 3 days, 40 mg. for 1 day, and 30 mg. for 6 days; treatment then was continued with 20 mg. of prednisone daily. The sodium and potassium level in the patient's serum was restored rapidly to normal, the general condition improved, and exact determination of blood pressure became possible again, with values of 105/80 mm Hg. There was prompt reduction of the absolute eosinophil values, and the hematocrit value was reduced to 34% volume. Additional sodium was administered to obtain sodium balance, which was reached after 14 days, when renal sodium excretion corresponded with the sodium supply. Excretion of sodium in the urine throttled immediately when the sodium supply was reduced to 7 gm. per day. This was considered as an indication that substitution therapy with prednisone was sufficient.

Studies of metabolism in 8 patients treated with prednisone did not reveal any disturbances in the electrolyte (water) metabolism. Glucose tolerance tests showed an increased blood sugar level after loading in 2 patients, but manifest diabetes mellitus occurred only in the patient who received combined treatment with corticotropin and prednisone. As a rule, one may not observe any influence on the electrolyte metabolism in persons with unimpaired adrenal cortex, although the diabetogenic effect of prednisone seems to correspond with that of corticotropin and cortisone respectively. The well-known risks associated with cortisone therapy (perforating ulcer, reduced defense power of the organism) must be likewise taken into consideration with prednisone therapy.

Pyogenic Pseudomyeloma of Bones. C. Jiménez Díaz, M. Morales Pleguezuelo and M. Ferrer Torrelles. Rev. clín. españ. **62**:219-224 (Aug. 31) 1956 (In Spanish) [Madrid].

The authors report a new type of chronic osteomyelitis that causes multiple tumors in the cranial bones and is due to the prolonged use of antibiotics administered in large doses. The only reference to this type of osteomyelitis in the literature is a single case reported in the American literature. The tumors are very painful. On histological examination they appear to be made up almost exclusively of plasma cells. Three cases are reported. The patients had had antibiotics in large doses and at frequent intervals for several years. The tumors developed in the skull in 2 patients and in the supraorbital bones in the 3rd. The supraorbital tumor caused loss of vision and of the eye, which had to be enucleated due to the unbearable pain. Pain in cranial bones and local complications after enucleation of the eye were controlled by erythromycin. The retro-orbital tumor and the tumors of the skull were formed almost completely from plasma cells. The osteomyelitis here described is due to the effect of antibiotics on staphylococci, which in turn alter the reaction of the plasma cells.

Clinical Experiences with Romicil (Oleandomycin), a New Antibiotic. P. Bünger and G. Schütze. Medizinische No. 51, pp. 1811-1816 (Dec. 22) 1956 (In German) [Stuttgart, Germany].

Oleandomycin (Romicil), a new antibiotic isolated from Streptomyces antibioticus, was given a therapeutic trial in 90 patients with suppurative processes, pneumonia, sore throat, abscesses, and other diseases caused by micrococci (staphylococci), streptococci, enterococci, and pneumococci, who were admitted to the Heidberg General Hospital in Hamburg, Germany, since August, 1955. The drug was available in tablet form and in dry-ampuls. Most of the patients were given oral treatment. The average daily dose was 33 mg. per kilogram of body weight in 4 or 8 divided doses; the smallest daily dose was 22 mg. and the

largest 60 mg. per kilogram of body weight. As a rule, 500 mg. was given 4 times a day. The highest total dose given to a patient with endocarditis was 96 gm., and 1 patient received 106 gm. in 2 courses. As a rule, the duration of the treatment was 8 or 10 days, and the average total dose administered was 20 gm. Only a few patients were given treatment parenterally by intravenous drip or intramuscularly with a daily dose of 1,000 mg. Tolerance of the drug when given orally was highly satisfactory. Therapy had to be discontinued in 2 patients because of an acute esophagitis. No change was observed in the intestinal flora even with total doses of 80, 90, or 100 gm. of the drug. Regular examinations of the blood and of the urine and liver-function tests did not reveal any changes for which the drug might have been responsible.

Excellent results were obtained in 58 of the 90 patients treated. Treatment with oleandomycin seems to be indicated in patients with pneumonia and bronchopneumonia, pulmonary abscesses, pleural empyema, furunculosis, abscesses, sore throat, staphyloderma, endocarditis caused by micrococci, suppurative parotitis, infections of urinary passage caused by micrococci, and ornithosis. Treatment was successful in two-thirds and in even up to 100% of the cases in which pneumococci, enterococci, or micrococci and streptococci, respectively, could be demonstrated. Sensitivity tests performed on primarily isolated bacterial strains and on those isolated in the course of and after treatment with oleandomycin showed that 95% of the bacteria with primary resistance to penicillin, streptomycin, and/or tetracycline were inhibited by oleandomycin. The good clinical results of treatment of patients with pneumonia, sore throat, furunculosis and abscesses, erysipelas, empyema, and endocarditis confirmed the results of the resistance tests. Three strains with primary resistance to erythromycin were also resistant primarily to oleandomycin, and 3 strains with primary resistance to oleandomycin were also resistant to penicillin and erythromycin. Bacteria in which secondary resistance to oleandomycin developed in the course of the treatment with this drug showed normal sensitivity to erythromycin. Bacteria with simultaneous resistance to penicillin, streptomycin, and/or tetracycline were inhibited by oleandromycin and maintained their primary resistance to the other antibiotics. Resistance to oleandomycin developed slowly and gradually, similar to that of the penicillin type. Treatment with oleandomycin, except by local application, does not offer much promise for success when bacterial growth is inhibited only by 3 mcg. or 6 mcg. per cubic centimeter. These findings suggest that oleandomycin is an antibiotic sui generis, despite the similarity of the spectrums of erythromycin, penicillin, and oleandomycin.

PATHOLOGY

Exfoliative Cytology in the Diagnosis of Lung Cancer: Examination of One Laboratory's Results. F. Hampson. Brit. M. J. **2**:1461-1462 (Dec. 22) 1956 [London].

A service in cytology was offered by the author's laboratory, and specimens of sputum were sent to it from a wide area, most of them coming from chest clinics and chest hospitals. The remainder were from general hospitals and general practitioners. All specimens had been collected by getting the patient to cough directly into a jar containing 70% alcohol. This routine is necessary only for specimens that cannot be examined at once. A total of 2,242 specimens from 1,019 patients was examined during the years 1952 to 1955 inclusive. The method is of great value in the diagnosis of lung cancer, especially in early cases. The positive results are reliable, and in accuracy it compares favorably with bronchoscopic examination. It is not intended that the study of exfoliated cells should replace any of the existing diagnostic methods but that it is a most useful additional aid. The method is simple and practicable for patient and clinician. No preparation of the patient is necessary; he does not have to attend hospital, and additional specimens can be readily obtained. For the laboratory the method has the advantage that no elaborate equipment is required, although experience is needed before confident results can be given.

Clinical Application of Gastric Cytology. R. E. Crozier, M. Middleton and J. R. Ross. New England J. Med. **255**:1128-1131 (Dec. 13) 1956 [Boston].

The studies reported were begun in January, 1955, at the Lahey Clinic. Inpatient studies were made at the New England Deaconess and New England Baptist hospitals. A few outpatients were studied at the Lahey Clinic. The present report covers the entire series of patients on whom the combined abrasion and lavage procedures were performed in the last 16 months. Although the authors were especially interested in obtaining patients thought clinically to have a malignant lesion, they accepted all patients in whom gastric disease was suspected, particularly neoplasm. In the 122 patients investigated the final diagnosis was ascertained by observation of response to medical therapy or by surgical exploration. The accuracy of results in gastric cytology is dependent upon the careful, rapid collection and processing of the material by well-trained personnel. Gastric lavage with isotonic sodium chloride solution is a simple, comparatively reliable method for cytological examination. Abrasive techniques did not prove to be as practical or reliable as gastric lavage. Gastric cytology is most useful to substantiate the clinical impression of a benign lesion, to enhance the clinical impression of a malignant lesion, and, on occasion, to diagnose an early, unsuspected gastric cancer.

Although cytological study is not a substitute for gastroscopy or roentgenography of the stomach as experience accumulates with this method, its position as a reliable supplement to other forms of investigation of gastric disease will become increasingly apparent. This study contributed to the diagnosis of cancer in 4 cases later confirmed by operation in which the x-ray diagnosis was benign disease or was equivocal, but more frequently it strengthened a clinical impression of a benign lesion, resulting in continued conservative management and the avoidace of surgery without harm to the patient. A prolonged follow-up study of these patients will be necessary before more definitive conclusions can be presented.

Stenosing and Obliterating Diseases of the Internal Organs. E. Asang and H. Mittelmeier. München. med. Wchnschr. **98**:1604-1609 (Nov. 23) 1956 (In German) [Munich, Germany].

The authors discuss the stenosing and obliterating diseases of the blood vessels on the basis of observations on 72 patients in whom the vascular disorder resulted in death and in whom the diagnoses were verified by autopsy. Stenosing and obliterating vascular diseases may take the form of an acute inflammatory reaction as well as the form of a sclerosis of the intima (atherosclerosis). Acute endangiitis and atherosclerosis are not fundamentally different processes but are phases of the same process. The so-called thrombangiitis obliterans is a thrombotic complication of endangiitis, not a special kind of vascular disease. The fact that the stenosing and obliterating vascular diseases are systemic has received insufficient attention, most reports being concerned only with limited vascular regions (such as the coronary arteries, brain, pulmonary circulation, and aorta). In emphasizing the systemic character of the obliterating vascular diseases the authors do not, however, imply that the entire vascular network is involved to the same degree; on the contrary, particularly in young persons, involvement of a single organ such as the heart or the kidneys may dominate the clinical picture.

They put special emphasis on the involvement of the vascular system of the intestines. In the patients they studied they observed endangiitis of the superior mesenteric artery in 56% of the patients, and in over half of these symptoms were present in the organs supplied by this artery. Impairment of its circulation causes attacks of "abdominal pains," which in analogy to "angina pectoris" may be designated as "angina abdominalis," or "claudication of the intestine," because it is comparable to intermittent claudication of the lower extremities. The resulting intestinal disturbances may take the form of constipation, or, more frequently, of sanguineous diarrhea, which may lead to the mistaken diagnosis of an intestinal infection. Severe stenosis or obliteration of the superior mesenteric artery may finally lead to intestinal infarction as the result of paralytic ileus. Some cases of acute pancreatic necrosis, splenic infarcts, many hepatic disorders, and gastrointestinal ulcers may also result from visceral endangiitis. The causes of death in the 72 patients with systemic endangiitis are tabulated in the following order of frequency: (1) intestine (infarction and ileus); (2) kidneys (uremia, hypertension, massive cerebral hemorrhage); (3) heart (coronary thrombosis, fibrosis, myodegeneration of the heart); (4) brain (malacia); (5) pancreas (necrosis); (6) lungs (failure of the right ventricle); and (7) aorta (ascending thrombosis, rupture of aneurysm).

The Pathomorphology of Pulmonary Tuberculosis: Investigations on Surgical Specimens. W. Masshoff. Deutsche med. Wchnschr. **81**:1873-1879 (Nov. 23) 1956. (In German) [Stuttgart, Germany].

The histopathological examination of a number of surgical specimens with various forms of pulmonary tuberculosis provided an opportunity for analyzing those factors and conditions that determine the behavior of pulmonary foci, particularly their spontaneous healing powers or their response to various forms of drug therapy. The fate of tuberculomas, also referred to as round foci, is determined not only by their size and bacterial content but to an at least equal extent by their relationship to the surrounding tissues, particularly to their bronchi. Solid or cavernous fibrocaseous processes, which are restricted to pulmonary segments or lobes, often show considerable fibrosis when they are removed after treatment with drugs. This fibrosis becomes manifest in foci of cicatrization in the parenchyma and in a nonspecific interstitial fibrosis. This interstitial fibrosis extends far beyond the focus itself. It has serious consequences, because the changes in the functioning component have secondary effects on the vessels and bronchi of the parenchyma. These secondary changes in turn may influence the primary parenchymal focus. The harmful effects of the interstitial fibrosis are most severe in the bronchi and are an important cause of the involvement of the bronchi, which often decides the outcome of the disease process.

Lateral Cervical Thyroid Metastases: A Follow-up Study of 39 Cases: (Aberrant Thyroid Tissue I). J. B. Dalgaard and P. Wetteland. Acta chir. scandinav. **111**:431-443 (No. 6) 1956 (In English) [Stockholm].

Forty-five biopsy specimens from lateral aberrant thyroid tumors in the neck obtained from 15 men and 24 women were studied at the department of pathology (Gade's Institute) of the University of Bergen, Norway. The 39 patients were traced and a follow-up study was carried out 1 to 24 years after they had been operated on for the first time. The age of the patients at the time of the operation varied from 22 to 89 years. The lateral tumors had been present from a few weeks to several years. Thirty-three showed a papillary structure, 4 were follicular, and 2 showed an undifferentiated small cell carcinomatous pattern. The follow-up study of the 39 patients revealed that a diagnosis of thyroid gland carcinoma had been established by microscopic examination of the homolateral thyroid lobe in 15 patients. A malignant growth of the thyroid gland subsequently had been diagnosed clinically in an additional 12 patients. The presence of carcinoma of the thyroid was not established by microscopic or clinical examination in the remaining 12 patients, whose average age was somewhat lower than in the 2 other groups. Thirteen of the 39 patients had died; death resulted from unrelated causes in 2 and from the malignant thyroid disease in 11. Most of the surviving 26 patients were well, although 5 of them had some recurrent lateral tumors. Seven patients were well who had undergone surgical removal of the lateral tumor but had not received any other treatment.

Two main concepts concerning the origin of so-called lateral aberrant thyroid tumors were proposed by various authors. The dysontogenetic theory maintains that the lateral aberrant thyroid tumors are developmental anomalies from alleged lateral thyroid anlages. Most of the workers favor the matastatic

theory, according to which the lateral thyroid tumors are metastases from thyroid gland carcinomas to the cervical lymph nodes. The authors' findings in the 39 patients strongly support the metastatic concept. A very protracted course is no real contraindication against a metastatic origin but only a peculiarity of the papillary thyroid carcinoma. It is this type of carcinoma that was found in 33 of the 39 patients and in most of those reported by other workers. Papillary thyroid tumors may show all grades of malignancy, but remarkably often the malignancy is low. These tumors often grow slowly and metastasize late and predominantly to the lateral cervical lymph nodes, i. e., just to the area in which the "lateral aberrant thyroid tumors" are found. The primary tumor in the thyroid gland may remain clinically "silent" for several years. The presence of a lateral cervical thyroid tumor is mostly an indication of a primary carcinoma in the homolateral thyroid lobe.

Hemithyroidectomy with removal of all lateral tumors is strongly advocated, but radical block dissection with removal of the sternocleidomastoid muscle seems unwarranted. Postoperative irradiation or treatment with radioactive iodine is recommended. The prognosis is not unfavorable, even in cases of recurrence.

RADIOLOGY

Selective Pulmonary Angiography. A. Actis-Dato, E. Minetto, P. C. Gamalero and R. Garbagni. Minerva med. **47**:1927-1935 (June 20) 1956 (In Italian) [Turin, Italy].

Selective pulmonary angiography was used to study the pulmonary vessels of a lobe or of isolated segments of the lungs in 15 patients with various pulmonary lesions. Selective angiography was used instead of total angiography because selective angiography points out much better the exact confines of pulmonary lesions that are to be removed surgically. The technique used was the same as that applied in cardiac catheterization. The patient is prepared by being kept at absolute rest and without any food for 6 hours. An injection of morphine or atropine is given 30 minutes before the examination. The catheter is introduced through the vena basilica isolated under local anesthesia with procaine hydrochloride and with the patient lying in the horizontal position. The radiopaque catheter of the Cournand type and of the largest possible size was used. The catheter, controlled fluoroscopically, is pushed into the atrium, the right ventricle, and into the pulmonary artery. The catheter is then maneuvered in a way that the apex should point toward that branch of the pulmonary artery in which the particular lobe to be studied is located. Possible occlusion of the catheter is prevented with a physiological solution of heparin. From 15 to 30 cc. of contrast medium is then injected through the catheter in a period of from 2 to 3 minutes. The injection is repeated after a few minutes, and other radiograms are taken with the patient in the laterolateral position with the side in which the pulmonary lesion is located near the radiographic plate.

Roentgen Therapy in Cushing's Syndrome Without Adrenocortical Tumor. F. C. Dohan, A. Raventos, N. Boucot and E. Rose. J. Clin. Endocrinol. **17**:8-32 (Jan.) 1957 [Springfield, Ill.].

Nine women and 3 men between the ages of 17 and 45 years with adrenal cortical hyperfunction (Cushing's syndrome) without detected adrenocortical tumor were given roentgen irradiation to the pituitary region at the department of radiology of the Hospital of the University of Pennsylvania in Philadelphia between 1932 and 1952. Multiple cross-firing portals were employed. Treatment was given 5 days a week. The total doses in "tissue roentgens" at the center of the pituitary fossa varied from 400 to 5,250. The total dose of the initial course of irradiation for the 5 patients who showed an excellent response was high, ranging from 3,800 to 5,250 tissue roentgens. The total dose for the 7 patients with a poor or fair response was lower, ranging from 400 to 4,550 tissue roentgens. Six of these 7 patients were subjected to one or more subsequent courses of irradiation, but with little effect. One patient apparently had a fair response after his 4th course of irradiation (965 tissue roentgens given at the mean rate of 138 r per day). Some signs of remission were usually evident within 3 months in the 5 patients who obtained excellent results, but marked improvement was not established earlier than 6 months after the initial roentgen irradiation. Hypophysial insufficiency occurred as a major complication of irradiation therapy in 1 patient who received a total dose of 3,800 tissue roentgens. The patient lost 30 lb. (13.6 kg.) in weight, had anorexia and weakness, and lost most of the hair on her face, arms, and legs. Five of the 7 patients with fair or poor response to the treatment died within 6 to 117 months after the initial roentgen therapy, and all 5 had cerebrovascular accidents.

Observations on the 12 patients and on 24 patients whose cases were collected from the literature suggest that the effectiveness of roentgen irradiation was better correlated with the mean dose of tissue roentgens delivered per day of the total course than with either total dose or duration of treatment. The estimated total tissue dose was plotted against duration of the roentgen therapy in days, on log-log paper. It was possible to draw a line that separated, in a highly significant fashion, the patients who responded from those who did not. Careful clinical trials should be made to test the hypothesis that Cushing's syndrome not associated with adrenocortical tumor will respond to a relatively low total roentgen dose delivered at a high average daily increment, such as 1,000 roentgens in 5 consecutive days or 1,500 tissue roentgens in 10 days with only 1 free-day interval.

Anomalies of the Thymus, Myasthenia Gravis, and Pneumomediastinography. M. Bariéty, C. Coury, and J.-L. Gimbert. Semaine hôp. Paris **66**:3445-3458, (Nov. 10) 1956 (In French) [Paris].

Insufflation of air into the superior mediastinum was carried out in 23 patients. A transtracheal route for the injection was used in 3 cases; in 14 the injection was made behind the sternum from above; in 5 it was made

behind the xiphoid process from below, and in 1 it was made from both above and below. The procedure, done under local anesthesia, was generally well tolerated. One patient, whose language difficulties had made it impossible to elicit a satisfactory history, had a convulsion but recovered promptly, so that the procedure was completed. Sweating and salivation, which always occurred together, were seen in 7 patients. The salivation was profuse for 3 or 4 minutes, was not prevented by premedication with atropine, and was particularly troublesome when it occurred in patients with myasthenia gravis who had difficulties with swallowing. Morphine should not be given in connection with this procedure. The needle was never inserted deeper than 1 cm. below the superior border of the manubrium sterni, and in no case was there evidence that the thymus had been punctured. The presence of about 250 cc. of air in the mediastinum does not always make a normal thymus visible. When the thymus was visualized, the resulting data as to its shape, location, and size were valuable.

Roentgenograms are given to illustrate the various conditions found in the 23 patients. Six had myasthenia associated with a previously recognized thymic tumor. Ten had thymic anomalies that could not be clearly revealed by ordinary roentgenography. In 4, pneumomediastinography made it possible to show that a suspected thymic anomaly did not exist. One thymic tumor was found in the absence of clinical signs of myasthenia, 1 endothoracic goiter was discovered, and in 1 case there was a technical failure. Altogether, 16 thymic anomalies were found among 22 patients with myasthenia.

Thymectomies were carried out in 10 patients with myasthenia and thymoma. There were 2 operative deaths, ascribed to inopportune use of curare. The operation caused no improvement in 5 patients. In 3 others, the operation, combined with radiotherapy, gave only partial, transient amelioration, so that medication with prostigmine had to be resumed.

ANESTHESIA

Analgesic Supplements to Nitrous Oxide Anesthesia: A Review. E. S. Siker. Brit. M. J. **2**:1327-1331 (Dec. 8) 1956 [London].

The ability to use nitrous oxide–oxygen as a safe general anesthetic was increased with the introduction of thiopental sodium. The advent of curare further widened the scope of anesthesia with nitrous oxide. Too much reliance on thiopental sodium supplementation led to frequent complications, while too much reliance on curare to maintain immobility led to the patient's awareness of the operative procedure during anesthesia with an otherwise inadequate anesthetic. Meperidine (Pethidine-Demerol) hydrochloride was originally used to increase the depth of anesthesia with nitrous oxide–oxygen. Investigations of meperidine hydrochloride as a supplement to nitrous oxide revealed many advantages associated with its use. Other narcotic analgesics such as levorphanol tartrate, alphaprodine hydrochloride, and the synthetic analgesic ketobemidone were soon investigated as supplements.

The lack of any clear-cut criterion for the assessment of analgesia in the course of general anesthesia was the great shortcoming throughout these investigations. Such clinically measurable values as the milligram per minute thiopental sodium requirements, the reaction time, and the duration of postoperative analgesia were used both to measure and to compare the efficacy of analgesic supplements. They gave valuable but incomplete information. Many narcotic analgesics were used successfully as a supplement to anesthesia with nitrous oxide. More precise methods for measuring the effects of these supplements in the course of anesthesia must be devised in order to get an idea of the proper role of these supplements in anesthesia, whether one drug is preferable to the other, or whether they need to be used at all.

Hypnosis in the Casualty Department. L. Goldie. Brit. M. J. **2**:1340-1342 (Dec. 8) 1956 [London.].

Hypnosis was used as an adjunct to or substitute for more conventional ways of producing anesthesia in unselected patients in the casualty department of a general hospital in London during April, 1954. There were 216 patients who required and had operations. Incisions were made in 59 of these patients, removal of a foreign body was carried out in 18, suturing in 95, reductions of fractures and dislocations in 38, and 6 patients were treated for nail avulsions. Hypnosis was used in 28 of the 38 orthopedic patients; 26 of the 28 were susceptible enough to allow a reduction to be performed; only 2 were failures, and these patients did not have fractures. This proportion was tested against the hypothesis that 4 out of 5 persons can be hypnotized. The observed proportion in the orthopedic patients exceeded it at the 5% level of significance. The patients requiring orthopedic treatment and those requiring suturing gave the best results with hypnosis, whereas profound anesthesia was less often produced in those whose injuries could for a time be left untreated, as those with abscesses and foreign bodies.

Hypnosis or suggestion may with advantage be used in the casualty department in the treatment of minor injuries. As an adjunct to the anesthetic facilities in the casualty department, it may reduce the number of anesthetics that need to be given and reduce the time spent in waiting for the digestion of a recently eaten meal or for the busy anesthetist occupied with major or more urgent operations. The technique is effective with untrained persons, especially those most likely to require an anesthetic. The author's observations, though not definitive, should redirect the attention to the need for more liaison between clinician, psychiatrist, and psychologist in the setting up of controlled scientific experiments in the environment of the general hospital. Hypnosis, like other techniques, varies with the skill and personality of the operator. The ideal is to minimize this factor by widespread use and training.

BOOK REVIEWS

The Principles and Practice of Medicine: A Textbook for Students and Doctors. By Sir Stanley Davidson, B.A., M.D., P.R.C.P., Physician to H. M. the Queen in Scotland, and Staff of Department of Medicine, University of Edinburgh, and associated clinical units. Third edition. Cloth. $8. Pp. 1076, with 74 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1956.

This is a book that should be most welcome among the myriad of large, and usually detailed, textbooks of general medicine. The emphasis is on the fundamentals of medical practice, that is, on the illnesses for which most patients seek professional care, and not on the rare and exotic maladies sometimes stressed in the schools. The subject matter is covered in what might be called an outline form, but at the same time it is far more complete than one's own clinical notebook. The systems of the body provide the subject matter of the major divisions of material, and, in addition, there is information on infectious diseases, chemotherapy, electrolyte balance, helminthic infestations, and nutritional disorders. The discussion of almost every disease manifestation includes a section on prevention and integrates this element of professional service as it properly should. The information on therapy is surprisingly up-to-date for a textbook, but, again, the emphasis is on the fundamentals of medical care rather than on the ever-changing concepts. At the end of each section there are references to easily available specialized information. The illustrations as well as the text material are clear, with illustrations in color where suitable. While it has many contributors, the book is really the product of a close-working team and reflects uniform, rather than competitive thinking. This uniformity is sometimes preferred in a basic or initial textbook on medicine because a homogeneous, and therefore more easily assimilable, foundation of knowledge is formed for the student.

Atlas of Tumors of the Nervous System. By H. M. Zimmerman, M.D., Chief, Laboratory Division, Montefiore Hospital, New York City, Martin G. Netsky, M.D., Professor of Neuropathology, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N. C., and Leo M. Davidoff, M.D., Attending Neurological Surgeon, Montefiore Hospital. Cloth. $25. Pp. 191, with 277 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1956.

The authors of this handsome atlas describe their book as a "partial substitute for the absence of a sufficient quantity" of cases of tumors of the nervous system in most clinics. Their aim is "to present the morphologic features of the tumors of the nervous system . . . as an aid in their diagnosis." In a brief introduction they state that they have adopted the classification of gliomas proposed by Bailey and Cushing "because it has been widely recognized . . . and a better . . . is not yet available." They criticize, somewhat unjustly, the simplification suggested by Kernohan and his group as disregarding the mixed nature of the gliomas, as being, in fact, not simpler, and as implying prophetic capacities of the pathologist with regard to malignancy. The book is divided into sections on the gliomas, meningiomas, neurinomas, tumors of the pituitary body, congenital tumors, sarcomas, tumors of the choroid plexus, and those arising in and from bone. There are added sections on metastatic neoplasms, granulomas, and tumors of the spinal cord, peripheral nerves, and sympathetic and paraganglionic cells. Each section is introduced with a brief, discriminating, and conservatively accurate discussion of clinical features and of macroscopic and microscopic appearance of the tumors in question. The illustrations are numerous and typical, without significant omissions, depicting both gross and microscopic appearances, and are chiefly in color. In conformity with the authors' opinion that most tumors of the nervous system can be identified with ordinary stains, they use the hematoxylin and eosin method predominantly, the phosphotungstic acid–hematoxylin method frequently, and other, including specialized, techniques rarely. A selective bibliography is presented that should be of great value to students, and an appendix gives statistical facts on the relative frequency of the various tumors and a tabular list of staining methods and their specific uses.

This atlas admirably fulfills its purpose. There is nothing quite comparable to it in print today. The nearest approach is the atlas "Tumors of the Central Nervous System," by Kernohan and Sayre, published by the Armed Forces Institute of Pathology, but the Kernohan-Sayre atlas omits coverage of the peripheral nervous system and its illustrations are only in black and white. This new atlas should prove invaluable to the general pathologist and to the beginner in neuropathology. As the authors clearly imply, no atlas can possibly portray the infinite variations in detail encountered in the daily study of tissues or supply the ability to discriminate that is won only from a rich and long experience. Nevertheless, as a representative and trustworthy guide, this atlas is superb. The reproductions in color are on the whole excellent. One notes some tendency for the reds to stand out at the expense of the blues, especially in the phosphotungstic acid–hematoxylin preparations, and the clearness of definition is not quite as sharp in color as we are accustomed to see in black and white. The latter defect is more than outweighed by chromatic verisimilitude. The text is a model of brevity and accuracy, with an unerring flair for the essential, a judicious presentation of the controversial, and a delightful simplicity of diction. Occasionally an important detail has been omitted, such as the role of the adrenal cortex in "Cushing's syndrome." The clinician should not look here for the minor details of symptomatology, but the pathologist should find what he needs of clinical facts. All these virtues, added to beautiful typography and attractive format, justify unreserved praise.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Roentgen Signs in Clinical Diagnosis. By Isadore Meschan, M.A., M.D., Professor and Director of Department of Radiology at Bowman Gray School of Medicine of Wake Forest College, Winston-Salem. With assistance of R. M. F. Farrer-Meschan, M.B., B.S. Cloth. $20. Pp. 1058, with 2216 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1956.

This book represents a new approach to diagnostic roentgenology. The material is organized by type of x-ray appearance, the objective findings as seen on roentgenograms, rather than by disease. By this method the reader is lead to organized thinking in the analysis of the roentgenographic findings and to a consideration of them in a differential manner, prior to arriving at a definite interpretation. In developing this type of approach, the author discusses the technical aspects, including positioning of the patient, exposures, contrast material, and the anatomy of the body region. For each disorder there is a clear, concise discussion of the roentgenographic appearance, pathological physiology of the lesion as it affects the appearance on the film, and the features that serve to aid in differentiating a particular disease from another. The concept of the author, in presenting and discussing the roentgenographic signs in this manner, can be exemplified in his consideration of bone disease under the headings of radiolucent bone diseases of multiple extremities and of a single extremity and of osteosclerotic and hypertrophic bone diseases of the extremities. Thus having determined the type of appearance and change, various diseases producing such findings can be considered.

The text is written in a clear and succinct manner, is well organized, reads like a novel, and is beautifully and completely illustrated. Although the reproductions of the roentgenograms are uniformly well chosen and of the highest quality, the diagrammatic sketches greatly enhance the value, conveying a superb conceptual idea of the abnormalities seen on the x-ray film. Adequate references are found at the end of each chapter, and the double-column index is most comprehensive. This excellent volume, written by an experienced teacher, is considered to be the most complete textbook of roentgenographic diagnosis ever published. The author is to be commended and congratulated. The manner of presentation is most logical and is in keeping with the methods used by outstanding teachers and preceptors. This book is recommended without reservation to all residents in radiology and allied specialties, and as a textbook for undergraduate teaching to be used after instruction in normal roentgenographic anatomy. All radiologists, particularly the teachers, should want to own this book. Any physician interested in diagnostic roentgenology should find it a useful guide.

Educating Spastic Children: The Education and Guidance of the Cerebral Palsied. By F. Eleanor Schonell, M.A., Ph.D. Cloth. $6. Pp. 242, with illustrations. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1956.

This excellent book has grown out of the author's experience among cerebral palsied children in Birmingham, England, supplemented by her experience in similar centers in Australia and New Zealand. In a field where many recent publications have been primarily a rehash of the literature or the restatement of pet theories—many of a controversial nature—it is refreshing to find a book that gives factual information and many practical suggestions.

Part 1 is a simple description of the medical aspects of the problem of cerebral palsy. The greatest contribution of the book is part 2, which is the result of the survey done in England on the intellectual capacity of cerebral palsied children. The author points out that neither the concept that all cerebral palsied children are feeble-minded nor the concept that all cerebral palsied children have normal intelligence is true. Her findings indicate that 50% of cerebral palsied children have an IQ of 70 or above. Another important point is that intelligence testing in cerebral palsied children is reliable in about 96% of the patients tested. The importance of these findings is that a realistic approach can be made to the educational problems of the 50% of cerebral palsied children for whom an educational program would be profitable. In part 3 the author gives some practical applications of the program. It was found that the severely handicapped educable palsied child, given the opportunity in a properly organized program, evidenced gratifying increases in the ability to read, to write, and to do arithmetic. Using specially devised reading and arithmetic tests, the author has been able to measure the progress of the students. Part 4 deals with some of the psychological and social aspects of the problem and covers them extremely well.

The book is complete, comprehensive, logical, and well written. The author does not pretend to make medical decisions, but she speaks with authority in the field in which she is qualified. The book is well supplemented with illustrations and with illustrative case reports. It also furnishes several valuable appendixes, with various sample forms used in the examinations, and also a comprehensive bibliography. It is written from the viewpoint of a practical person, imbued with the curiousity of the researcher. It is to be highly recommended for physicians, educators, and administrators interested in the education of the cerebral palsied child.

Diabetes Mellitus: Handbook for Physicians. By Howard F. Root, M.D., Sc.D., F.A.C.P., Medical Director of Joslin Clinic, Boston, and Priscilla White, M.D., Sc.D., F.A.C.P., Instructor in Pediatrics, Tufts University, Boston. Cloth. $7. Pp. 346, with 6 illustrations. Landsberger Medical Books, Inc., distributed solely by Blakiston Division of McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36, 1956.

This is a practical manual for the guidance of physicians in the detailed use of current clinical methods of diabetic management. Emphasis is on treatment; many chapters open with a brief discussion of the nature of the condition to be treated. The great variety of complications related to diabetes is discussed from a rich background of experience by both authors. For the most part the methods discussed are those used at the Joslin Clinic. Now and then, however, some awareness of experience and methods used elsewhere is shown. In this book Dr. White reiterates her contentions regarding the controversial question of hormonal inbalance and replacement therapy in pregnant

diabetic women. As evidence of the success of such therapy, a fetal mortality rate of 32% among 154 women who reached the 28th week of pregnancy without the use of female sex hormones is compared to a rate of only 12% among 710 women who did receive endocrine therapy. The contrast was fully as great for the entire period of pregnancy, with the worst results in both treated and untreated patients occurring among those with the most severe diabetes and those with the most severe vascular and renal disease. It is not clear whether the treated and untreated groups were comparable in all respects other than hormone therapy. If the groups were not comparable, the results given do not mean much; indeed, they may be misleading.

Other more common problems of diabetic management are covered in a practical manner and in great detail. Results of oral therapy with hypoglycemic sulfonylurea compounds are described. For the most part the authors tell the physician what to do rather than why to do it. From this standpoint the volume is a harmless companion to their well-known textbook that covers the same ground but usually gives reasons for doing so. It is doubtful that the small price difference between the two books makes this one an object of choice. The other gives much more information, is better written, and should be useful much longer.

Industrial Deafness: Hearing Testing and Noise Measurement. By Joseph Sataloff, M.D., D.Sc., Assistant Professor of Otology, Jefferson Medical College of Philadelphia. Cloth. $8. Pp. 333, with illustrations. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E.C.4, England, 1957.

This compact volume is part primer, part manual, and part textbook. Its author directs the book to otologists, hearing testers, industrial physicians, industrial executives, compensation lawyers, insurance executives, acoustical engineers, safety engineers, chambers of commerce, industrial nurses, industrial hygienists, and labor union leaders. No single volume could appeal in its entirety to such disparate groups. It is of interest superficially to the first, generally to the second, universally to the third, and only in small measure to the latter nine. The author has had wide experience in the field of acoustic trauma and sets forth his treatise knowledgeably and with clarity. As a primer it is basic but not boring in its consideration of the fundamentals of sound, hearing, and deafness. As a manual it is an inclusive but uncluttered guide to the determination of acoustical danger in any given industrial noise level. As a textbook this volume is as thorough as brevity will allow.

The role of each member of the team in the detection of impaired hearing and in the conservation of hearing in industry is delineated. Methods of early diagnosis are stressed. Prophylaxis, the only satisfactory approach, is discussed. Special sections deal with the handicapping effects of deafness, the effects of noise on human behavior, medicolegal aspects of acoustic trauma, and damage-risk criteria. Individual susceptibility to acoustic trauma is recognized, but no mention is made of possible methods for its detection on the screening examination, such as the test for decreased linear range of hearing. This test is already in use in one of our largest industries. The book ends with an entertaining and effective article directed to the noise-exposed worker and entitled "What a Hearing Conservation Program Means to You." It augurs well for the ears of the plant whose industrial physician extends his acquaintance with industrial deafness to include this volume.

Diseases of the Heart and Circulation. By Paul Wood, O.B.E., M.D., F.R.C.P., Director, Institute of Cardiology, London, England. Second edition. Cloth. $15 (U. S. market only). Pp. 1005, with illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Eyre & Spottiswoode, Ltd., 14-16 Bedford St., Strand, London, W.C.2, England, 1956.

The author has, over the course of years, gained wide experience as a cardiologist. Thus, his book reflects to a large measure his own work rather than a review of the literature. The text is clearly written and well illustrated. Although the word "circulation" in the title suggests that a section on peripheral vascular disease might be included in the book, such is not the case. The author states in the preface that such a section was originally contemplated but abandoned because so many excellent monographs are already available on the subject.

This edition has been completely rewritten to include the recent advances in cardiology. Thus in the section on congestive heart failure such drugs as Mictine and Diamox are discussed; under rheumatic fever the use of benzathine penicillin as a prophylactic agent is described; and recent research on the role of fat in the diet is summarized in the chapter on ischemic heart disease. Although there is no special chapter on surgical treatment of cardiac disorders, the indications and possible benefits from operation are considered under each condition. The author must have expected that his book would appeal to American physicians, because he has been careful to note where American practice differs from British practice, particularly in relationship to drugs. The section on electrocardiography is short but adequate for a general textbook on heart disease. There is a well-written chapter entitled "Special Investigations." Here are described such tests as cardiac catheterization, measurements of venous pressure, circulation time, and blood volume determinations. References are given at the end of each chapter. This is an excellent, up-to-date reference book on diseases of the heart for the general practitioner or the internist.

Ocular Surgery. By H. Arruga, M.D. Translated from fourth Spanish edition by Michael J. Hogan, M.D., Clinical Professor of Ophthalmology, University of California School of Medicine, San Francisco, and Luis E. Chaparro, M.D. Second English edition. Cloth. $48. Pp. 948, with 1309 illustrations. McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E.C.4, England; Salvat editores, S.A., 41-49 Calle de Mallorca, Barcelona, Spain, 1956.

The new edition of "Ocular Surgery" in English should receive acclaim not only in our country but in every country in which English is spoken or read. This world-famous author has collected the most practical

techniques of other ophthalmologists, interspersed them with his comments, appraisals, and criticisms, and added his personal approach to these same problems. He describes a new operation (dacryorhinostomy) for persistent lacrimation even after dacryocystectomy. Not only is this procedure not impossible, as it would appear at first mention, but the results are generally successful. The other refreshingly new procedures and devices described are (1) the ingenious Strampelli technique for placing the plastic lens in the anterior chamber, (2) Shapland-Paufique's operation for inferoexternal lamellar scleral resection, (3) the unique and clever Champignotom and Lamellarotom of Franceschetti, used to obtain a perforating full-thickness corneal graft centrally, and a peripheral lamellar graft (mushroom graft), and (4) the Arruga-Maura-Brazil implant in enucleation. This monumental volume includes classic and colorful photographs of operations for retinal detachment, corneal grafts, lid repair, strabismus, and cataracts.

The translators are to be highly commended for their success in conveying the exact meaning of the original Spanish text. The tremendous and extensive clinical and surgical background of the author, together with his methodical, step-by-step photographs, drawings, and diagrams, should make this the most sought-after book and reference work in ophthalmological circles.

A Manual of the Common Contagious Diseases. By Philip Moen Stimson, A.B., M.D., Professor of Clinical Pediatrics, Cornell University Medical College, New York, and Horace Louis Hodes, A.B., M.D., Pediatrician-in-Chief and Director of Department of Pediatrics, Mt. Sinai Hospital, New York. Fifth edition. Cloth. $8.50. Pp. 624, with 93 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1956.

This excellent book brings together most of the significant information available today concerning the common contagious diseases. The material is presented in a clear, concise, and useful manner. The opening chapter deals with the principles of contagion and immunity. In the second chapter the authors discuss in detail serum reactions and their treatment. In the third chapter they discuss the currently available antibiotics and sulfonamides used in the treatment of contagious diseases. The next 12 chapters are devoted to a detailed discussion of the contagious diseases, including etiology, pathology, diagnosis, and treatment. Then follows a chapter concerning the general management of contagious diseases including such details as the management of contagious diseases in hospitals and an outline of medical aseptic technique. This chapter is followed by a glossary and an index. The authors clearly indicate at the beginning that they are dealing only with contagious diseases and that they are not attempting to discuss all diseases classified as infectious. A minor criticism might be offered concerning the discussion of the treatment of diphtheria. It is suggested that, if penicillin is found ineffective when the patient is in the carrier state, one of the tetracyclines might be substituted. Available information at present would seem to favor the administration of erythromycin in such instances. This book can be recommended highly to the teacher, student, and practitioner.

The Visual Fields: A Textbook and Atlas of Clinical Perimetry. By David O. Harrington, A.B., M.D., F.A.C.S., Clinical Professor of Ophthalmology, University of California School of Medicine, San Francisco. Cloth. $16. Pp. 327, with 243 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1956.

This monograph represents the most important contribution to the literature on the visual fields since the monumental presentation of this subject by Traquair and his popularization of quantitative perimetry. There have been new developments since 1948, when the last edition of Traquair's "An Introduction to Clinical Perimetry" appeared, and the author has covered these most adequately. Retaining the concept of the visual field as an "island of vision surrounded by a sea of blindness," and reemphasizing the necessity of careful quantitative determinations of the peripheral and central field defects, the author has described some of the more recent methods of examination. These include the extinction phenomenon, examination with ultraviolet radiation and luminous test objects as introduced by him, angioscotometry as advocated by Evans, flicker fusion fields, and the multiple-pattern method for quick screening. As is imperative in a book that describes visual fields in a wide variety of ocular and neurological conditions, there are copious original drawings and field charts, many of which correlate the site of the lesion with the perimetric studies. These are accurately and clearly depicted and, together with the lucid and informative text, tend to make this a book that should be in the library of every ophthalmologist, neurologist, and neurological surgeon. There is a bibliography of 133 references, but few readers will seek more information than is included in the text.

How to Enjoy Good Health. Edited by Cyril Solomon, M.D., and Brooks Roberts. With introduction by George F. Lull, M.D., Secretary-General Manager, American Medical Association. [Many of these articles were published originally in *This Week Magazine*.] Cloth. $3.95. Pp. 240. Random House, Inc., 457 Madison Ave., New York 22, 1954-1956.

In the introduction to this book is the statement, "The continually increasing amount of space given in the press to medical articles testifies to the unquenchable thirst of American readers for such information. In mass-circulated magazines alone, some 450 medical stories were published last year." The editors have attempted to quench this thirst by collecting in this volume 66 articles on medical subjects that originally appeared in *This Week Magazine*. The articles are grouped into three sections: "Keeping Healthy Day by Day," "Special Situations and Problems," and "Disease and Your Body." The subjects extend from allergies to virus and from anemia to weather. Each essay is by an authority in the field, including men serving in the various bureaus of the American Medical Association. All are written in a clear, simple, and interesting manner and show a remarkable consistency in form and structure, an example of good editing. This volume can be recommended to patients who want authoritative information in easily understandable language. It should be a valuable addition to high school and college libraries as collateral reading in hygiene courses. The medical columnist and the health officer with a voluminous correspondence should find it a useful, authentic aid in answering their mail.

Minimal Pulmonary Tuberculosis Found by Mass Radiography (Fluorography). Report to Prophit Committee, Royal College of Physicians, by V. H. Springett, M.D., M.R.C.P., and including results of work done by A. J. Eley, M.A., M.B., B.S., Director, Ministry of Health Mass Radiography Unit, London. Cloth. 42s. Pp. 233, with 81 illustrations. H. K. Lewis & Co., Ltd., 136 Gower St., London, W.C.1, England, 1956.

A five-year follow-up was made of 500 presumably healthy persons of each sex found by mass radiography to have small tuberculous lesions in the lung. The survey included a study of the clinical, bacteriological, and radiologic records of the patients. An assessment of the prevalence of minimal lesions was not the main purpose of this study, but mass radiography offered a convenient method of collecting information about a suitable and adequate number of patients with such lesions who could be followed up for five years. Over 180,000 persons, ranging in age from 15 to 44 years, were examined. Among these were 1,213 persons with minimal lesions. This excellent report contains an abundance of interesting and valuable information dealing not only with the detection of lesions but also with definitive diagnosis and management. It should be of great interest to all physicians concerned with the diagnosis and treatment of tuberculosis.

Etiologic Factors in Renal Lithiasis. Compiled and edited by Arthur J. Butt, B.S., M.D., F.A.C.S. Cloth. $12.50. Pp. 401, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1956.

This book is an excellent résumé of suspected etiological factors in the development of renal stones. The organization of the book, from its opening chapter on historical survey through the various metabolic, infectious, geographical, and chemical theories that have been propounded, is good. Much of the information, and particularly that on chemistry, is theoretical, but the work as a whole is a satisfactory summary of our current knowledge of certain facts, with a comprehensive evaluation as to possibilities of further study. The relationships of infection, obstruction, and stasis are well explained and summarized. Attention is called once again to some of the factors that are so significant in the development of recurrent calculi. The value of the work to the general practitioner will be limited; to the general urologist, less limited; and, to the researcher in the field of urinary stones, it should be of considerable value.

A Scientific Sampler. By Raymond Stevens, Howard F. Hamacher and Alan A. Smith. Cloth. $6. Pp. 413, with 1 illustration. D. van Nostrand Company, Inc., 120 Alexander St., Princeton, N. J.; 25 Hollinger Rd., Toronto 16, Canada; Macmillan & Co., Ltd., St. Martin's St., London, W.C.2, England, 1956.

This book consists of a series of essays on science written in a way that makes it readable to either the layman or the specialist. It covers many fields and in it may be found information on such diverse subjects as anthropology, sensations, sugar, brain food, morale, hobbies, and imagery. The book is based on articles that have been published in the *Industrial Bulletin of Arthur D. Little, Inc.* over the years. While interesting, the statements are more entertaining than informational. Unquestionably there are many statements that can be quoted and to which reference can be made, but it is not a technically prepared book in the sense that textbooks are. It is the sort of book that one reads primarily for enjoyment, yet with the thought that useful informaion will be accumulated. It lends itself to the armchair or bedside table rather than to the research desk.

The Support of Medical Research. Edited by Sir Harold Himsworth, Chairman of Conference, and J. F. Delafresnaye, C.I.O.M.S. Symposium organized by Council for International Organizations of Medical Sciences, established under joint auspices of U.N.E.S.C.O. and W.H.O. Cloth. $4. Pp. 170. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B. Canada, 1956.

This volume is the report of a conference held at the Royal Society of Medicine, London. It includes an account of the discussions and appendixes containing statements about the arrangements for medical research in the countries represented at the meeting. It also includes a bibliography. It is not a formal report, but an expression of views by those attending the conference, and in this respect it offers interesting information for reference.

Comyns Berkeley's Pictorial Midwifery: An Atlas of Midwifery for Pupil Midwives. Revised by D. M. Stern, M.A., M.B., Ch.B., Consulting Obstetric and Gynaecological Surgeon to West Middlesex Hospital and Chiswick Maternity Hospital, London. With additional drawings by Susan Robinson, M.M.A.A., Medical Artist, West Middlesex Hospital. Baillière's Handbooks for Nurses. Fifth edition. Cloth. $3.75. Pp. 164, with 224 illustrations. Baillière, Tindall & Cox, 7-8 Henrietta St., Covent Garden, London, W. C. 2, England; Williams & Wilkins, Mount Royal and Guilford Aves., Baltimore 2, 1956.

This comparatively small book obviously will have limited usefulness in the United States. However, medical students and even some general practitioners will find it an understandable, easily read book whose value rests on its excellent illustrations. There are more than 200 of these figures depicting situations commonly encountered in obstetric practice. Accompanying many of the figures are brief explanatory comments that are concise but clear.

Your Adolescent at Home and in School. By Mary and Lawrence K. Frank. Cloth. $3.95. Pp. 336. Viking Press, Inc., 18 East 48th St., New York 17; Macmillan Company of Canada, Ltd., 70 Bond St., Toronto 2, Canada, 1956.

This book was written for parents, teachers, and others interested in adolescent boys and girls. It is not technical and is easy to read. Perhaps its greatest appeal to the reader lies in the approach taken by the authors. They explain the problems that arise in such a way that the reader becomes familiar with the situations and thus becomes cognizant of the various facets of adolescent development.

QUERIES AND MINOR NOTES

ANTIBIOTICS IN MILK

To the Editor:—*In the Nov. 10, 1956, issue of* The Journal, *under Queries and Minor Notes, it was stated that antibiotics, if present in the flesh of fowl and fish, were destroyed in the process of cooking. Has there been any work on the use of milk and eggs as a vehicle for antibiotics? Many patients have rashes that look like drug rash, and yet there is no history of any medication. Could there be any connection?*

Jackson Herbert, M.D., Portsmouth, Ohio.

This inquiry has been referred to three consultants, whose respective replies follow.—Ed.

Answer.—The question of the presence of antibiotics in foods has been of serious concern to biological scientists, animal husbandmen, and public health officials since the discovery that antibiotics are of value as therapeutic or prophylactic agents and growth stimulants in domestic animals. The problem was discussed at length at the First International Conference on Antibiotics in Agriculture in October, 1955. These discussions have been published (National Academy of Sciences–National Research Council Publication 397, 1956). There was not complete unanimity. Some research workers believe that continued use of antibiotics in meat animals or on meat products may result in the development of resistant micro-organisms or otherwise adversely affect the consumer. The great majority of research workers are on record as saying that antibiotics do not constitute a problem to humans if correctly used. Either the use of so called "low-level" antibiotic feeding to animals producing meat, milk, or egg or the dipping of fish or chickens in solutions containing antibiotics produces no antibiotic retention, or else the amounts retained are quickly destroyed in cooking.

The use of "high-level" or therapeutic doses of antibiotics may result in considerable antibiotic activity of milk. Mastitis is a widespread disease of dairy cattle. The infusion of the udder with antibiotics is a common treatment and is carried out by both veterinarians and lay personnel. Veterinarians usually recommend that milk not be used for human consumption for at least 72 hours after the injection of a therapeutic agent. When antibiotics in oily or waxy bases are infused into the udder, the milk should be discarded for 72 hours. There have been instances when milk containing antibiotic activity has entered commercial channels and numerous cases where cheese manufacture has been affected by such activity. Guaranteeing that therapeutic agents will be used in accordance with recommendations is difficult if not impossible.

This problem has been reviewed by Doan (*J. Dairy Sc.* **39**:1766, 1956). A 1954 survey of antibiotic activity of 94 samples of market milk showed that 3.2% contained activity. A nationwide survey of 474 samples in 1955 showed that 11.6% contained antibiotic activity. Responsible dairy leaders warn that continued carelessness and sometimes unwarranted use of antibiotics in the treatment of mastitis must cease. There is circumstantial evidence that antibiotics in milk could be responsible for some of the allergic reactions that occur in man.

It was reported by Greiff and Pinkerton (1951) that the feeding of antibiotics of the tetracycline type to hens produced eggs with some resistance to rickettsial growth. However, Wong and associates (1953) fed hens up to 1,000 gm. of oxytetracycline and penicillin per ton of feed without producing an antibiotic effect in the eggs. This level of feeding is many times greater than would be used in commercial poultry.

Answer.—Three surveys (Welch and others: *Antibiotics & Chemother.* **5**:571, 1955; ibid. **6**:369, 1956) by the Food and Drug Administration have been made to determine the content of antibiotics in fluid market milk. The first survey showed that 3.2% of 94 samples tested contained penicillin. In the second survey, 474 samples of market milk were tested and 11.6% were found to contain penicillin. The concentrations in the milk varied from 0.003 to 0.08 units per milliliter. In the third survey, 1,706 samples were examined and these were collected from all of the 48 states and the District of Columbia. This extensive survey showed penicillin in concentrations of 0.003 to 0.550 units per milliliter in 5.9% of the samples tested. In addition, one of the penicillin-positive samples apparently contained streptomycin and 17 additional samples (approximately 1%) appeared to contain bacitracin, one of the tetracyclines, or a combination of these drugs. It is believed the presence of penicillin in milk is caused by the farmer's sending milk to the dairy sooner than 72 hours after treatment of the mastitic cow with an antibiotic preparation, which is contrary to the directions contained in the labeling of these drugs.

As a result of these surveys, the Food and Drug Administration held a meeting with a Medical Advisory Panel, representatives of the Animal Health Institute, Associated Veterinary Laboratories, American Drug Manufacturers Association, American Veterinary Medical Association, Milk Industry Foundation, Food Protection Committee of the National Research Council, American Medical Association, and the Department of Agriculture to discuss the public health significance of antibiotics in milk. In general, it was agreed that penicillin, because of its sensitizing action, might produce a public health problem. It was recommended that studies be made to try to find out the quantity of penicillin in milk that would cause a reaction.

It is believed that if the farmer or milk producer is educated to discard milk from cows treated for mastitis for a 72-hour period after the last treatment and

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

if the label of the immediate container of the drug contains such a warning statement, the presence of penicillin in milk can be eliminated. Also, it has been suggested that the maximum amount of penicillin per dose should be limited to 100,000 units. Some preparations now on the market contain as much as 1,500,000 units per dose. Proposed regulations incorporating these suggestions are now under consideration.

A small survey on eggs was conducted by the Food and Drug Administration several years ago. Ninety samples, including shell eggs, broken whole eggs, egg whites, and egg yolks, from six different areas, were examined, and none was found to contain penicillin. Four of the samples (one broken whole egg and three egg whites) were found to contain some substance that inhibited the growth of micro-organisms, but this substance could not be identified as an antibiotic. Occasionally, natural substances have been found in egg whites that inhibit the growth of micro-organisms.

ANSWER.—No experimental work appears to have been reported in which an individual sensitive to a specific antibiotic was challenged with milk or eggs from animals or birds receiving that antibiotic. As ordinarily marketed milk from cattle is pooled, antibiotics in milk from one animal become diluted. Thus, it is unlikely that any considerable number of eruptions is due to or maintained by antibiotics in milk. In any patient with a prolonged eruption as from penicillin, it would be relatively easy to eliminate questionable foods in order to put the hypothesis in the query to a test.

TUBERCULIN TEST IN MILIARY TUBERCULOSIS

TO THE EDITOR:—*What is the proportion of positive to negative tuberculin tests in those with miliary tuberculosis?*

S. Theodore Sussman, M.D., New Rochelle, N. Y.

ANSWER.—No reference has been found to a large series of persons with miliary tuberculosis tested with tuberculin. However, enough testing has been done and the pathogenesis of the disease is so well understood that it can be stated that practically all cases develop in allergic tissue, which would, therefore, react to tuberculin if tested just before the miliary disease develops. Miliary tuberculosis is caused by a lesion, often primary, located adjacent to a lymphatic or blood vessel, that invades the wall and discharges its tubercle bacilli in tremendous numbers into the lymph or blood stream. The bacilli are rather promptly lodged in various organs, including lungs, kidneys, spleen, and even the brain. This condition may occur soon after primary lesions are established or at any subsequent time in the individual's life, including old age. In persons who have not previously been tested with tuberculin, miliary disease may be the first manifestation of tuberculosis. Primary lesions resulting from the initial infection with tubercle bacilli usually result in a degree of allergy sufficient to be elicited by the tuberculin test within three to seven weeks after the invasion occurs. Miliary disease may develop soon after allergy is established. For example, an infant may be infected on the first day of life and develop miliary disease at the age of 3 or 4 weeks or subsequently. In such cases, tuberculin testing usually has not been done and, therefore, the allergy was not known to exist. If the patient is seen soon after the massive numbers of tubercle bacilli enter the lymph or blood streams, the tuberculin reaction can nearly always be elicited. As the disease progresses, however, in many cases allergy wanes and reaches such a low level that it is not detected by the standard first dose and, in some cases, even the second dose of tuberculin. However, if sufficiently large doses are administered, tissues will react, since they never completely lose their refractoriness to tuberculin. In overwhelming acute forms of tuberculosis, including meningitis, miliary disease, and pneumonia, as well as chronic forms in the terminal stage, the tissues may become so desensitized that if only the usual test doses of tuberculin are used the allergy is not elicited.

The tuberculin reaction and recovery of tubercle bacilli are the only two specific findings to justify the diagnosis of miliary tuberculosis. In the past, when the tissues had become so desensitized that there was no reaction to the usual test doses of tuberculin the physician was at a loss to make a diagnosis of miliary disease. Observing miliary tubercles in the retina was helpful, as well as seeing evidence of them in lungs from their x-ray shadows. Inasmuch as in approximately one-half of the cases of generalized miliary tuberculosis the pulmonary tubercles do not cast x-ray shadows, at least that fraction of the cases were diagnosed only at autopsy in the past. Steiner showed that, as long as the tubercles are epithelioid, they cast no shadow on x-ray films. Shadows are cast only by those that contain collagen or caseous material.

Prior to the advent of antituberculosis drugs, prompt diagnosis of miliary tuberculosis was not as important as now, because the disease was universally fatal. Soon after streptomycin was produced, Scleicher found that a high percentage of persons with generalized miliary tuberculosis, with or without x-ray shadows of tubercles in the lungs or in the retina, had numerous small granulomas in bone marrow. These were found to contain tubercle bacilli. This finding is now regarded as specific evidence of presence of generalized miliary tuberculosis even in the absence of x-ray shadows or reaction to the usual test doses of tuberculin. Therefore, when generalized miliary tuberculosis is suspected, bone marrow studies should be made. Antituberculosis drugs, especially isoniazid, have a markedly suppressive effect on tubercle bacilli in generalized miliary tuberculosis. However, their usefulness diminishes rapidly with progression of the disease. Therefore, in a person of any age with symptoms suggestive of miliary tuberculosis who has not previously been tested with tuberculin and who now fails to react to the usual test doses, bone marrow findings may promptly justify the diagnosis so that treatment can be instituted when it is of most avail.

OCCLUSIVE VASCULAR DISEASE

To the Editor:—*A 66-year-old woman first had coronary insufficiency in 1936. Since then she has had several episodes, with favorable responses to conventional therapy. Except for precordial distress, this patient at no time complained of anginal syndrome, contralateral radiation of pain, or radiation of pain along the inner aspect of the left arm. She sometimes takes 1/100 grain (0.6 mg.) of glyceryl trinitrate (nitroglycerin) sublingually, mainly in anticipation of effort. In 1953, she had had what was considered a small, transient cerebral vascular thrombus, with no premonitory symptoms. At examination her blood pressure values are within normal range, her weight is 130 lb. (59 kg.), and her pulse rate is 72 per minute. An electrocardiogram taken in April, 1956, demonstrated a healed anterior wall myocardial infarction. Now there is sudden onset of numbness, pain, and coldness of the toes in the left foot of two to three weeks' duration. She also complains of "an inner coolness in the left leg." The big toe is more sensitive than the other toes. She has none of these symptoms while walking around in the house. Symptoms suggestive of intermittent claudication were elicited. There is pallor on elevation and some rubor on dependency. Posterior tibialis and dorsalis pedis arteries are not palpable. In the absence of symptoms of diabetes mellitus, should the diagnosis be that of an ischemic foot? She has varicosity of both legs; should a phlebothrombosis of one of the deep veins be considered? Does phlebothrombosis of the lower extremities bear a relationship to coronary insufficiency? Would oscillometry aid in making a more accurate diagnosis? Are vasodilators indicated, and which would be recommended? Would some sort of an elastic stocking be of help in the treatment?*

A. J. Ishlon, M.D., Miami, Fla.

Answer.—This patient has evidence of previous arteriosclerotic disease, on the basis of both her coronary symptoms and the cerebrovascular accident. The symptoms of sudden onset of numbness and pain and coldness of the toes of the left foot of two to three weeks' duration, along with the absence of posterior tibial and dorsalis pedal artery pulsations, would be sufficient evidence to make the diagnosis of an acute occlusion of the major arterial supply in the leg. Pallor on elevation of the extremities and prolongation of the venous filling time beyond 25 to 30 seconds when the foot is in a dependent position also helps to confirm the diagnosis of arterial insufficiency. Incompetent varicose veins will shorten the venous filling time. If pain and numbness persist, the diagnosis of ischemic neuritis can be made, and it could be considered an ischemic foot. In the absence of swelling and local evidence of any thrombophlebitis, it is doubtful that phlebothrombosis of the deep veins needs to be considered as a cause of her problem. Phlebothrombosis of the lower extremity does not bear any relation to coronary insufficiency, with the exception of coronary insufficiency and cardiac failure with dependent edema, in which condition phlebothrombosis may be a complication. Oscillometry is an aid to confirm the physical findings but is not necessary for a more accurate diagnosis. If the patient has persistent pain, if the dorsalis pedal and posterior tibial pulses are absent, and if the foot blanches when elevated and the venous filling time is prolonged when the legs are held in a dependent position, one can, in general, assume that the patient has occlusive arterial disease of a significant degree. If an oscillometer is applied to the calf and there is an absence of oscillations, this merely confirms the physical findings of occlusion of the major arteries.

While the use of vasodilator agents is of questionable value, they should be tried. Priscoline, Ilidar, Arlidin, Roniacol, and nicotinic acid are some drugs used. The injection of one of these drugs into the femoral artery if it is patent is frequently more effective than oral administration. Intra-arterial injections can be given daily for a period of three to five days, but after this additional injections may damage the artery at the site of injection. Elastic stockings, in general, are of no help, and the patient will complain that the pain is increased by them. In vascular problems, one should never rule out the possibility of diabetes on random determination of sugar in urine or blood samples. It is necessary to do a glucose tolerance test with a test one-half hour, one hour, and two hours after 100 gm. of glucose has been given orally. Treatment of choice, once the diagnosis of occlusive vascular disease and ischemic neuritis has been confirmed, is a lumbar sympathectomy if the patient is not a diabetic. The sympathectomy is the best means this consultant has found to relieve the ischemic pain. If the pain is not relieved by a sympathectomy, the prognosis is very poor and the patient will soon require amputation of the extremity because of the severity of the pain or because of gangrene, which will usually soon follow.

TOXOPLASMOSIS OF THE EYE

To the Editor:—*Is there any available information relative to establishing the diagnosis of a chronic toxoplasmosis involving the posterior uveal tract of the eyes? What treatment may be used?*

J. C. Damitz, M.D., Akron, Ohio.

Answer.—Except in congenital infections Toxoplasma does not produce ocular damage as commonly as current opinion might lead one to believe. Feldman was able to demonstrate Toxoplasma antibodies in only 18 of 140 suspected cases of postnatally acquired toxoplasmic chorioretinitis. In verified toxoplasmosis involving the eye there may be a history of acute retinitis or, less often, of uveitis, or the inflammatory process may develop gradually. Characteristically, in acquired, as distinguished from congenital, infections, it tends to become chronic as the involved cells change their role from host to that of phagocyte, with corresponding decrease in multiplication of Toxoplasma organisms and frequently their inclusion in pseudocysts. From these pseudocysts the infection may later become reactivated.

Three immunologic tests have been developed for toxoplasmosis. The intradermal reaction, which may be of some value in determining group incidence of the infection, is not recommended for specific cases. Both the dye test and complement-fixation reaction are reliable serologic indicators of toxoplasmic antibodies. The former requires living Toxoplasma grown in laboratory mice or in tissue culture to test antibody formation in the patient's serum, and the latter requires an experimental source for antigen. Feldman states that "antibodies are usually detectable by the dye test within two weeks after onset of the infection and persist in diminishing titer for many years, if not for life," while "complement-fixing antibodies develop somewhat slowly, requiring about a month or more to reach their peak levels and then diminish sharply or disappear within two to four years." Utilization of both these serologic techniques in suspected infections has definite diagnostic advantages. Specific chemotherapy is still on a clinically experimental basis. Sulfadiazine, sulfamethazine, and sulfamerazine in tolerated doses tend to inhibit development of the toxoplasma organisms. Pyrimethamine (Daraprim) has definite promise of antitoxoplasmic activity and appears to have a synergistic effect when combined with the sulfonamides. Obviously granulomatous changes and calcification will not be materially altered by toxoplasmicidal or toxoplasmistatic drugs.

DOUBLE UTERUS AND VAGINA

To the Editor:—*A young woman, age 19 years, has had dysmenorrhea becoming much more severe in the past 12 months. Her previously regular menstrual periods have become somewhat irregular, the flow being prolonged at times and varying from 6 to 12 days in duration. Pelvic examination was formerly impossible because of a virginal introitus with an intact hymen. Hymenotomy was done, and the patient was found to have a septum dividing the vagina into two channels. There is a small cervix at the vault of each of these vaginal channels, and hysterosalpingography revealed that there are two uteri, each with a patent tube. There is no communication between the two uterine cavities or endocervical canals. The uteri appear hypoplastic. What is the proper term for this duplication, which seems to be complete with the exception of the tubes? How frequently does this anomaly occur? What may be predicted as to this young woman's ability to conceive and to carry a pregnancy to term? In view of her intention to marry within six months, how should she and her prospective husband be advised? What kind of plastic surgical procedure, if any, is indicated? Is the problem described rare enough to warrant thorough studies, with pictures and x-rays, and reporting?* *M.D., Montana.*

Answer.—The condition described is known as uterus didelphys or uterus duplex, bicornis cum vagina septa. The exact frequency with which this anomaly occurs is not known. However, Smith (*Am. J. Obst. & Gynec.* **22**:714, 1931) found one case of uterus didelphys in every 70,973 deliveries. He said that a double uterus of some type, exclusive of simple septate vagina and uterus arcuatus, was found once in every 1,500 pregnancies. Fenton and Singh (*Am. J. Obst. & Gynec.* **63**:744, 1952) found 62 congenital malformations of the uterus and vagina among 60,788 deliveries, or 1 in 633 deliveries. Of course there are some women with uterine anomalies who never marry, never conceive, or have abortions only. In most cases of uterus didelphys with septate vagina there is no difficulty in having intercourse because one vagina is larger than the other and is ample for coitus. This is why septate vagina is often overlooked by patients and even by physicians. Women with double uteri are highly fertile. Pregnancy may occur in one or both horns. If each horn contains an ovum, the two children may theoretically have been conceived at different impregnations and be delivered at different times, thus suggesting superfetation. When pregnancy occurs in one horn it is ordinarily undisturbed; the side not involved grows and forms a decidua similar to that in ectopic gestation. The decidua of the empty side may be cast out while the pregnancy continues on the other side. It will appear that the patient has had an abortion, and unless the existence of a double uterus is known the physician will curet and unwittingly destroy a living ovum. Usually the decidua sloughs away in the puerperium with the lochia.

Labor is usually normal, but the following complications have been observed: weak pains, atony with postpartum hemorrhage in the third stage, and adherent placenta. The nongravid portion of the uterus may prolapse under the other and act like an incarcerated tumor. The uterus may rupture because of poor musculature, and the septum in the vagina may act as an obstruction. Septate uteri may have the following complications: breech and transverse presentation, premature rupture of the membranes, weak pains, postpartum atony, rigidity of the cervix, an adherent placenta on the septum, and, if the septum is in the cervix, obstruction to delivery. During pregnancy, because of the frequency of abortions, the patient's activities should be restricted, especially around the time the menses would have appeared. During labor the patient must be watched closely. Malpresentations are common and may be the deciding factor for cesarean section. Likewise, the possibility of a weakened uterine musculature must be remembered; therefore, all patients with a double uterus should be delivered in a hospital. Usually delivery can be accomplished safely from below either spontaneously or with aid. At the time of labor a cervical or vaginal septum should be removed. This may be done when the presenting part pushes the septum almost into view or after the baby is delivered. Certainly if the septum is a hindrance to the exit of the baby it should be incised or excised. The third stage is usually normal, but one must be prepared for hemorrhage from the weak musculature and from a retained placenta.

If it appears that the patient will be able to have intercourse by means of one or both vaginas, nothing need be done. If, however, the septum will prevent coitus, it can easily be removed surgically. A long clamp is placed on the upper part of the septum near

the bladder from the introitus to the cervix, and another clamp is placed on the lower part of the septum near the rectum. The intervening septal tissue can be removed with an electric cautery or by excision with scissors and sutured with surgical gut. In view of the fact that this patient is only 19 years old, the dysmenorrhea should be treated conservatively. The prolonged flow at the menses may be due to the fact that the bleeding occurs from two uteri instead of one.

It might be advisable to study the urinary tract in this patient by intravenous pyelography, because malformations of the urinary tract often accompany genital deformities. The case is worthy of a report with hysterograms, but preferably after the patient has had a pregnancy.

PROLONGED STEROID TREATMENT OF ASTHMA

To the Editor:—*A 10½-year-old boy has suffered from asthma since he was 8 months of age. One of numerous pediatricians and allergists he has consulted believed him to be allergic to streptococci and staphylococci in his respiratory system. He has had allergens prepared from secretions from his nose, throat, and bronchi, and a complete course of desensitization has been carried out, without benefit. For the past six years the boy has continuously taken cortisone, hydrocortisone, and, lately, prednisolone. The mother now has the dosage reduced to 1.25 mg. of prednisolone twice a day. She recognizes the dangers of continuous dosage but states that skipping a single dose precipitates an attack of asthma. The child is checked regularly and shows no signs of water retention, Cushing's syndrome, or adrenal suppression. He has never had corticotropin (ACTH) in conjunction with the above medication. Please suggest the advisability of concomitant use of corticotropin and, if possible, outline a new course of treatment.*

Frank McGreane, M.D., Calistoga, Calif.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—The problem as posed here is occurring with increasing frequency and underscores the advisability of not starting hormone treatment for chronic allergic diseases. Not only is it exceedingly difficult to stop the use of such potent hormones, but such therapy of asthma and other allergic disturbances materially increases the difficulty in treating such hormone-treated patients. This is unfortunate, for there is as yet no adequate substitute for making a specific diagnosis in allergy and then either having the patient avoid the incriminated materials or treating him specifically. Substituting a maintenance dose of corticotropin for prednisolone should be tried in the hope that this might stimulate adrenal function. Sometimes the dosage of corticotropin may then be tapered off gradually after a few weeks. But if it becomes impossible to eliminate the use of the drug, as is often the case, then there is no alternative to attempting to make a specific diagnosis of allergy, even if this has to be done while the patient is receiving a maintenance dose of prednisolone, corticotropin, or both. Sometimes hormone therapy cannot be eliminated until at least a part of the allergic load is detected and specific exposures are reduced.

In the making of the specific diagnosis of allergy, skin-testing procedures are reliable only as far as pollens, dusts, danders, and other extracts of inhaled particles are concerned. Skin testing in food allergy is not recommended, but sensitivity to foods is a common cause of asthma in childhood. Specific food allergy is determined by performing individual food tests with the most commonly eaten foods. This list usually includes wheat, corn, milk, egg, potato, orange, and others, depending upon the child's eating habits. The technique of the individual food test (Rinkel and coworkers: Food Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1950) consists of the complete avoidance of one or more suspected foods for at least four days and then their return to the diet one at a time. Incriminated or asthma-inducing foods are avoided as detected. Elimination diets of the type popularized by Rowe (Elimination Diets and the Patient's Allergies: Handbook of Allergy, ed. 2, Philadelphia, Lea & Febiger, 1944) are also helpful.

Answer.—From the evidence at hand, there would be no indication for either concomitant or intermittent administration of corticotropin. In these situations, many allergists and pediatricians realize that a calculated risk must be taken, with the dangers of almost continuous asthma in a developing youngster weighed against those inherent in the prolonged intake of steroids. The present consensus is that clinical disuse atrophy is not averted by the administration of corticotropin and that small doses of prednisolone are well tolerated by these patients if certain safeguards are observed.

The patient should be meticulously checked at regular intervals by thorough physical examination, with complete blood studies. Rigid observation during periods of infection and/or other forms of stress must be carried out; intensive antibiotic therapy plus supportive measures, including additional steroids, if indicated, should be utilized. Continued attempts to definitively ascertain offending allergens in order to effect either elimination or desensitization must not be abandoned. The ingestion of corticosteroids should be brought to an end as soon as clinically possible.

PREFRONTAL LOBOTOMY IN CHILDREN

To the Editor:—*Has prefrontal lobotomy ever been applied to children? I have in mind a child who is extremely belligerent, hyperkinetic, and severely mentally retarded. Tranquilizers have been of no value.*

M.D., Michigan.

Answer.—Mental retardation can sometimes be simulated in a child as the result of unfavorable human environment. Even if there is severe mental retardation on an organic cerebral basis, persistent belligerence and hyperkinesis might well be related to some chronic personal problem. Often a change of environ-

ment with provision of affectionate nursing care produces worthwhile results. In any event, pediatric psychiatric guidance should be sought, perhaps through the Neuropsychiatric Institute of the University of Michigan at Ann Arbor. Where behavior disorders of a child are involved, a prudent physician would not ordinarily recommend surgical operation on the brain (with the possible exception of a hemispherectomy in the case of unilateral cerebral atrophy marked by frequent uncontrollable focal seizures and hemiparesis as well). A frontal lobotomy sufficient to affect hyperkinesis and belligerence would be too extensive and destructive a procedure in the case of a young person, where the potential for recovery is so great.

NEWCASTLE DISEASE IN MAN

To the Editor:—*A patient gave a history of having gone into a chicken house after it had been dusted with Newcastle disease vaccine, B-1 strain, and infectious bronchitis vaccine (live virus dust). He then developed a virus infection of the lungs and has not completely recovered at the present time. Are there any cases reported in which this live virus vaccine has caused any diseases in humans, and, if so, what are the symptoms?*

Melvin C. Bowman, M.D., Neosho, Mo.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—The vaccine in question is for the purpose of immunizing poultry against two avian infections, infectious bronchitis and Newcastle disease (pneumoencephalitis). To accomplish this end, the vaccine contains living but attenuated strains of the etiological agents involved. There appears to be no record in the medical literature of infection in humans caused by the virus of infectious bronchitis. The virus of Newcastle disease has been known to cause an acute granular conjunctivitis of short duration in some nonimmune persons. The conjunctivitis is occasionally accompanied by fever, chills, headaches, and malaise. For this reason, the manufacturer strongly recommends the use of gargles and a mouth and nose wash when spraying. The virus has not been shown to be involved in severe or chronic respiratory infections. For the above reasons, it is unlikely that the respiratory symptoms described can be attributed to the vaccine.

Answer.—Newcastle disease has been recognized in man since the original report by Burnet, in 1942, of a case resulting from accidental spraying of the eye with infected chorioallantoic fluid of an embryonated egg. With the subsequent identification of numerous cases of human infection throughout the world, the original tendency to dismiss it as a transient and inconsequential "disability," chiefly involving the conjunctivas, has been modified. The principal clinical manifestations as described by Quinn and co-workers (*J. Lab. & Clin. Med.* **40**:736, 1952) are malaise, conjunctivitis, ulceration of the buccal mucosa, and preauricular lymphadenopathy. The onset occurred 18 to 24 hours after accidental exposure of five patients, whose history and clinical manifestations were studied closely. Newcastle disease virus was recovered from the conjunctival sac washings, saliva, blood, nasal discharges, and urine from one or more of these patients. The virus was recovered from the bronchial secretions of a patient who developed bronchitis following exposure to the virus. A strain of virus was isolated from human lung tissue.

Various reports emphasize the occupational occurrence of Newcastle disease among persons in contact with naturally and vaccination-infected poultry, among poultry eviscerators in packing plants, and among laboratory workers, especially those preparing and testing commercial living Newcastle disease vaccines. While lower respiratory tract involvement in cases of this disease has apparently been uncommon, the nature of the virus together with its wide spectrum of affinity for species as well as different tissues of the body must place it in a suspect position. The suggestion of Quinn and co-workers in 1952 that Newcastle disease "may have greater significance for man than is generally recognized" certainly warrants critical study of all known or suspected cases, especially those in which there are manifestations other than those so far associated with the disease.

HAZARD OF PARAKEETS IN HOSPITALS

To the Editor:—*Does keeping parakeets in cages in the corridors of a hospital constitute a hazard to patients in adjacent rooms? What are the possibilities of transmitting infection from birds to patients by personnel who attend both? Is there any way of detecting incipient psittacosis in birds? What is the length of time after which infection transmitted to patients might cause clinical symptoms?*

M.D., Illinois.

Answer.—There is danger in keeping parakeets in cages in the corridors of hospitals. The psittacosis virus is present in the nasal secretions and droppings of the birds. It gets on their feathers and contaminates their cages and when dried may pollute the air that circulates in their cages. It is perfectly possible for persons handling the birds or their cages to contaminate food and bed linen of patients in close proximity if the attendants do not observe careful infectious technique. The incubation period is said to be 7 to 15 days. Since antibodies against psittacosis virus usually require several weeks to reach their maximum titer, there is no way of detecting "incipient" psittacosis before the birds manifest illness.

IMPOTENCE AND RESERPINE THERAPY

To the Editor:—*A 37-year-old man with essential hypertension took reserpine (Serpasil) for three months (0.25 mg. four times a day). He complains that since he began taking reserpine he has been unable to have an erection. Is it common for reserpine to have this effect?*

M.D., Missouri.

Answer.—Sexual impotence is not found among the generally recognized undesirable side-effects of reserpine therapy. It is not included among the untoward effects of the drug listed in N. N. R. 1956. Wilkins

(*Ann. New York Acad. Sc.* **59**:36, 1954) states "The slowness of action of the drugs [Rauwolfia] has suggested that they work through some hormonal or other intermediate mechanism. One hormonal route readily and currently suggested is the adrenal cortex, particularly through the sex-stimulating steroids. There is some clinical evidence for this in men who uniformly comment, if not complain, about a decrease in libido while taking the drug. This, however, is definitely not impotence, and two young men have fathered new babies while on the drug." Kline (*Ann. New York Acad. Sc.* **59**:107, 1954) refers to a 1931 report on Rauwolfia by Sen and Bose in which these authors apparently mentioned the "marked depressive action" of the drug on the sexual centers. However, Kline, in reporting his clinical experiences with the Rauwolfia preparations, stated that "there was no evidence of decrease in sexual activity and, in fact, several of the patients reported unusually erotic dreams."

PENICILLIN DESENSITIZATION

To the Editor:—*Is it possible to desensitize people to penicillin?* *R. J. Sexton, M.D., Charleston, W. Va.*

This inquiry has been referred to two consultants, whose respective replies follow.—Ed.

Answer.—There is no practical reliable method of desensitizing penicillin-sensitive patients. The fractional method of desensitization, even where effective, would take too long to be of any practical value. This procedure is not without danger in patients anaphylactically or atopically sensitive to penicillin. It is suggested that some other suitable antibiotic be substituted where penicillin sensitivity is suspected.

Answer.—Desensitization to penicillin has been reported following the use of various techniques. However, it is difficult to evaluate these procedures, since it is not uncommon for a sensitive patient to become spontaneously desensitized. A patient in whom further treatment is indicated, as in syphilis, may develop urticaria after the institution of penicillin therapy, but often continued administration of this antibiotic fails to cause an exacerbation of the hives. Furthermore, as treatment is continued the reaction is apt to subside. Especially with the use of antihistaminics and corticosteroids, practically any such patient can be treated with penicillin to a successful completion of his course of therapy.

LARGE THYROID PRESENT AT BIRTH

To the Editor:—*What is the clinical significance of a diffuse thyroid enlargement in a 5-lb. (2,267.9-gm.) premature (36 weeks) baby? It is neither cystic nor adenomatous. Is this common? What treatment is indicated?* *M.D., Wisconsin.*

Answer.—Occasionally infants are born with goiters if the mother was taking an antithyroid drug during pregnancy. The goiters in these children disappear spontaneously soon after birth. Congenital goiter occurring spontaneously may be an indication of hypothyroidism, and the enlargement of the thyroid under such circumstances represents a compensatory reaction to the hypothyroidism. The treatment is administration of desiccated thyroid in a dose of at least 1 grain (60 mg.) daily, increasing to 2 grains (0.12 gm.) of a standard U.S.P. noncoated thyroid preparation if the goiter does not decrease in size when 1 grain is given. Acquired goiters in infants have also been noticed in patients taking artificial milk formulas and cobalt preparations. These goiters disappear promptly when the child is given thyroid. Diffuse enlargements of the thyroid in an infant or newborn child are usually compensatory reactions to a thyroid deficiency and can be corrected by thyroid feeding.

ONE OVERACTIVE THYROID AREA

To the Editor:—*Reports come from isotope laboratories that there is often one area of hyperactivity in an otherwise essentially normal thyroid when tested with radioactive iodine. If the total radioactive iodine uptake is within normal limits with such a patient, would the patient be considered to have significant thyroid disease if one localized area were quite "overactive" as far as the radiation count is concerned?* *Warren F. Wilhelm, M.D., Kansas City, Mo.*

Answer.—Not many clinicians would be willing to make a diagnosis of hyperthyroidism on the basis of an increased radioactive iodine uptake, whether this is localized or diffuse in the thyroid. There are many factors that affect uptake of radioactive iodine, and it is only one of many useful laboratory tests in determining the presence or absence of hyperthyroidism. The fact that one nodule in the thyroid is more radioactive than other parts does not necessarily indicate that hyperthyroidism is present or that it will develop. This merely signifies that one area is carrying the greatest burden of work in producing thyroid hormones and that the rest of the gland is in a more or less resting phase.

SIMPLE RETAINED PLACENTA

To the Editor:—*What is the possibility of recurrence of simple retained placenta in a woman aged 28, whose retained placenta was uncomplicated and uninfected? The present pregnancy is her second.* *William R. Watson, M.D., Watford City, N. D.*

Answer.—Since recurrence of a simple retained placenta is not frequent and since the condition itself does not carry any danger, there is no need for worry. Today there is much less reluctance to manually remove a placenta than there was formerly. Therefore, if a placenta remains in the uterus for more than 20 minutes and if the physician is experienced, the placenta should be removed manually in one piece. Of course, if there is bleeding, the placenta should be removed earlier.